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SEVERE PRE-ECLAMPSIA WITH PARTIAL HELLP SYNDROME IN MULTIGRAVIDA PRETERM PREGNANCY

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ABSTRACT
Preeclampsia is the second highest cause of maternal death in Indonesia. The incidence of preeclampsia in Indonesia is very high at 24%. West Java is a province in Indonesia with a high preeclampsia rate of 25%.Pre-eclampsia is a vascular endothelial dysfunction and vasospasm that occurs at gestational age above 20 months and is characterized by hypertension and proteinuria, with or without pathological edema. Severe preeclampsia (PEB) is characterized by a minimum of systolic blood pressure 160 mmHg or diastolic blood pressure 110, impaired liver function, progressive renal insufficiency, pulmonary edema, brain and visual disturbances, or thrombocytopenia. This research is descriptive observational with a case report approach. The aim of this research is to discuss updates on the occurrence, concept, pathophysiology, and management of preeclampsia. In the case reported, a female patient, aged 29 years G3P2A0, 36 weeks gestational age with severe pre-eclampsia, partial hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome in a multigravida preterm pregnancy with grade I obesity and a history of cesarean section 5 years ago. After evaluation, the patient complained of headache and heartburn. After confirmation, the fetus has IUGR, then active management with Transperitoneal Sectio Caesarea is chosen.

Keywords: HELLP syndrome; IUGR; multigravida; preeclampsia

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INTRODUCTION

Severe preeclampsia (PEB) is the first cause of high maternal and child mortality and morbidity in developing countries. The incidence of severe preeclampsia reaches 8% of all pregnancies in the world (Abalos, 2013). Preeclampsia is the second highest cause of maternal death in Indonesia. The incidence of preeclampsia in Indonesia is very high at 24% (Kemenkes RI, 2017). Pre-eclampsia is a disorder in which vascular endothelial dysfunction and vasospasm occur after 20 weeks of gestation and can persist for up to four to six weeks after delivery. In general, preeclampsia is associated with hypertension and proteinuria, with or without edema, in pregnancy. In cases of preeclampsia, systolic blood pressure above 140 mmHg or diastolic pressure above 90 mmHg, in two consecutive examinations within an interval of four hours in previously normotensive patients.

Whereas in severe preeclampsia, systolic blood pressure is above 160 mmHg and diastolic blood pressure is above 110 mmHg (Lim, K. H., 2019) If the gestational age has reached 37 weeks or above, the treatment carried out by health workers is termination of pregnancy.

Meanwhile, if it is under 37 weeks, if there are no complications, the baby is still maintained while PEB is carried out (Leeman et al, 2016). One of the main PEB protocols given is the initial administration of MgSO4 followed by maintenance. However, giving MgSO4 can only be done if it meets the requirements, namely the availability of calcium gluconate antidote, respiratory rate above 16 times per minute, positive patellar reflex, and good urine output (Sibai, B. M., 2014). In this study, we will discuss cases of severe preeclampsia with partial HELLP Syndrome so that active management must be carried out. The aim of this research is to discuss updates on the occurrence, concept, pathophysiology, and management of preeclampsia

METHOD

This research is descriptive observational and case report. The subjects of this study were a female patient, aged 29 years G3P2A0, 36 weeks gestational age with severe pre-eclampsia, partial hemolysis, elevated liver enzymes, and low platelet count (HELLP) syndrome in a multigravida preterm pregnancy with grade I obesity at Dr. Hospital. H. Abdul Moeloek. Primary data analysis was obtained from anamnesis, physical examination, and laboratory investigations. Evaluation and examination were carried out on November 29, 2021 to December 1, 2021. The results of the study were analyzed using scientific journals obtained from google schoolar, PubMed, NCBI in the last 10 years. the keywords used are Severe preeclampsia with Partial HELLP Syndrome.

RESULTS

A 29-year-old G3P2A0 woman with 36 weeks of gestation came to the Emergency Unit of Abdul Moeloek Hospital, Lampung Province with a referencediagnosis G3P2A0 36 weeks of gestation with Preeclampsia (PEB) + history of Caesarean section 5 years ago + IUGR. The patient presented to our hospital with 2 days of worsened headaches, all over the head, came and went, improved with rest, disturbed the patient's sleep. The patient had never experiences shortness of breath and blurred vision. The patient complained of nausea and vomiting ± 3 times, nausea felt intermittent, vomit filled with water. The patient complained of pain in the pit of the stomach since ± 2 days ago. The patient's mother had a history of hypertension. The patients never had history of diabetes mellitus, asthma, allergies, heart disease. Patients routinely did Antenatal care at the midwife every month and perform ultrasound at the specialist Obstetrics-Gynecology 3 times during pregnancy.

Physical examination results revealed hypertension (blood pressure 186/114mmHg) with pulse and respiration within normal limits. Body mass index 30.8 kg/m2 (obesity grade I). Examination of the head and thorax within normal. Abdominal examination revealed a single intrauterine fetus, elongated with head presentation, head has not entered the pelvis with HIS (-), Fetal heart rate 138x/minute, uterine fundus height 28 cm, Estimated Fetal Weight 1635 grams. Examination of the genitalia revealed blood (-) discharge (-). Blood laboratory examination showed an increase in AST: 109 U/L, an increase in ALT: 69 U/L, and an increase in LDH 738 U/L. Hemoglobin, platelets, urea and creatinine are within normal limits. Urinalysis examination revealed proteinuria 500 mg or +2. Ultrasound examination revealed a single intrauterine fetus, fetal heart rate (+), BPD 8.64, AC 27.33 cm, FL 6.70 cm. From the ultrasound results, it was found that the fetus had Intrauterine Growth Restriction.

The patient was diagnosed with Severe PE with partial HELLP Syndrome in multigravida preterm pregnancy, with a history of CS 5 years ago, with grade I obesity. The patient was then planned for active management with PEB procedures (O2 3 liters per minute, IVFD RL + MgSO4 40% 6 grams IV for 6 hours 28 drops per minute, Injection of MgSO4 40% 4

grams diluted with 10cc aquabides, Methyldopa 3x500mg orally). plus the administration of 1 ampoule of Dexamethasone/12 hours for 2 days for surfactant maturation. The patient was then planned for Emergency SCTP. After the Emergency SCTP was performed, the patient still had hypertension. then the patient received additional therapy with nifedipine 3x10 mg. On the 2nd and 3rd day of post-SC treatment the patient improved, blood pressure had dropped, and from the laboratory examination, the patient's AST, ALT and LDH levels were normal. Urinalysis did not reveal proteinuria. The patient was then discharged on day 3 post CS.

DISCUSSION

Hypertension is one of health problems that often appears in pregnancy and often causes complications. The incidence of hypertension in pregnancy is around 5-15% and is one of the causes of morbidity and mortality in pregnant women and childbirth in addition to bleeding and infection. Hypertension in pregnancy can be classified into: Chronic Hypertension, Gestational Hypertension, Preeclampsia-Eclampsia, Chronic Hypertension with Superimposed Eclampsia (POGI, 2016) Chronic hypertension is hypertension that occurs before 20 weeks of gestation or hypertension that is diagnosed for the first time after 20 weeks of gestation and hypertension persists until 12 weeks postpartum. The diagnosis is made if blood pressure is 140/90 mmHg, history of hypertension before pregnancy, or had hypertension before 20 weeks of pregnancy without proteinuria (POGI, 2016; Sofie, R.K., 2019).

Gestational hypertension is hypertension that occurs in pregnancy after 20 weeks without proteinuria and hypertension disappears after 3 months postpartum. The diagnosis is made when blood pressure is 140/90 mmHg without proteinuria, there is no history of hypertension before pregnancy, and can be accompanied by signs and symptoms of preeclampsia. (POGI, 2016; Sofie, R.K., 2019) Preeclampsia is hypertension that occurs after 20 weeks of gestation accompanied by proteinuria 300 mg/24 hours or 1+ on dipsticks. Meanwhile, eclampsia is preeclampsia accompanied by seizures (POGI, 2016; Sofie, R.K., 2019). Chronic hypertension accompanied by superimposed eclampsia is chronic hypertension accompanied by signs of preeclampsia or chronic hypertension accompanied by proteinuria during pregnancy (POGI, 2016; Sofie, R.K., 2019).

Pre-eclampsia usually occurs after 20 weeks gestation and is a multi-system disorder. It was classically defined as a triad of hypertension, oedema, and proteinuria, but a more modern definition of pre-eclampsia concentrates on a gestational elevation of blood pressure together with 0.3 g proteinuria per 24 hours. Oedema is no longer included because of the lack of specificity. Pre-eclampsia may also manifest, with few maternal symptoms and signs, as isolated intrauterine growth restriction (IUGR). Eclampsia is defined as the occurrence of a grand mal seizure in association with pre-eclampsia, although it may be the first presentation of the condition. The risks to the fetus from preeclampsia include growth restriction secondary to placental insufficiency, and premature delivery. Indeed, pre-eclampsia is one of the most common causes of prematurity (accounting for 25% of all infants with very low birth weight 1500 g).

Several theories about the causes of preeclampsia are:

Placental vascular

Abnormalities In normal pregnancy, the uterus and placenta receive blood flow from the uterine and ovarian arteries. The two blood vessels penetrate the myometrium in the form of the arcuar artery and the arcuar artery giving off the radial artery. The radial artery penetrates

the endometrium to become the basal artery and the basal artery gives rise to the spiral arteries. In normal pregnancy, the cytotrophoblast villi invade the muscle layer of the spiral arteries, causing degeneration of the muscle layer, so that the spiral arteries lose their endothelium and most of their muscle. Invasive trophoblasts also enter the tissue around the spiral arteries so that the matrix becomes loose and makes it easier for the spiral arteries to dilate and distend. Distension and vasodilation of the spiral artery lumen results in a decrease in blood pressure, vascular resistance, and an increase in blood flow in the uteroplacental area. As a result, blood flow to the fetus is quite a lot and tissue perfusion is also increased, so as to ensure good fetal growth. This process occurs remodeling of the spiral arteries. In gestational hypertension, trophoblast cell invasion does not occur in the muscle layer of the spiral arteries and the surrounding matrix tissue. The muscle layer of the spiral arteries is still stiff and hard so that the lumen of the spiral arteries does not allow for distension and vasodilation. As a result, the spiral arteries experience vasoconstriction and failure of spiral artery modeling occurs, resulting in decreased uteroplacental blood flow, and placental hypoxia and ischemia (Sofie, R. K., 2019).

Placental ischemia, free radicals, and endothelial dysfunction

In hypertension during pregnancy there is incomplete spiral artery remodeling causing the placenta ischemia. Ischemia of the placenta will produce oxidants (called free radicals). One of the oxidants produced is hydroxyl which is very toxic, especially to the endothelial cell membrane of blood vessels. Hydroxyl radicals will damage cell membranes, which contain a lot of unsaturated fatty acids into fatty peroxides. Fat peroxide in addition to damaging the endothelial cell membrane, will also damage the nucleus, and endothelial cell proteins, will also damage the nucleus, and endothelial cell proteins (Sofie, R. K., 2019). In hypertension in pregnancy it has been proven that levels of oxidants, especially fatty peroxides increase. Fatty peroxides as oxidants will circulate throughout the body in the bloodstream and will damage endothelial cells. Endothelial cell membranes are more susceptible to damage because they are in direct contact with the bloodstream and contain lots of unsaturated fatty acids. Unsaturated fatty acids are very susceptible to hydroxyl radical oxidants, which will turn into fatty peroxides (Sofie, R. K., 2019). As a result of endothelial cells exposed to fatty peroxides, there is damage to endothelial cells, which damage starts from the endothelial cell membrane. Damage to the endothelial cell membrane results in disruption of endothelial function, even the destruction of the entire structure of endothelial cells, which is called endothelial dysfunction. This situation results in Impaired prostaglandin metabolism, because one of the functions of endothelial cells, is to produce prostaglandins, namely decreased production of prostacyclin (PGE2) a strong vasodilator. Aggregation of platelet cells in damaged endothelial areas (sofie, R. K., 2019).

Genetic Theory

There are hereditary and familial factors with a single gene model. The maternal genotype determines the occurrence of familial hypertension in pregnancy when compared to the fetal genotype (Sofie, R. K., 2019).

Nutritional Deficiency Theory

Several research results show that nutritional deficiency plays a role in the occurrence of hypertension in pregnancy. Recent studies have shown that consumption of fish oil, including halibut oil, can reduce the risk of preeclampsia. Several studies have also shown that calcium deficiency in the diet of pregnant women results in the risk of preeclampsia (Sofie, R. K., 2019). Trophoblast Stimulus Theory This theory is based on the fact that the release of trophoblastic debris in the blood circulation is the main stimulus for the inflammatory

process. In normal pregnancy, the placenta also releases trophoblastic debris, as the remains of apoptotic and necrotic trophoblasts, as a result of oxidative reactions that are still within normal limits. Whereas in preeclampsia there is an increase in oxidative stress, so that the production of apoptotic and necrotic trophoblast debris also increases. The more placental trophoblast cells, for example in large placentas, in multiple pregnancy, the oxidative stress reaction will greatly increase, so that the amount of trophoblastic debris remains also increases. This situation creates a burden of inflammatory reactions in normal pregnancy. This inflammatory response will activate endothelial cells, and larger macrophage/granulocyte cells, resulting in a systemic inflammatory reaction that causes symptoms of preeclampsia in the mother (Sofie, R. K., 2019).

The diagnosis can be made by history taking, physical examination and supporting examinations. These results have shown the correct diagnosis, namely G3P2A0 36 weeks pregnant with PEB + Partial HELLP Syndrome in multigravida preterm pregnancy with grade I Obesity + IUGR. From history taking, she complained dizziness since two days before admission to the hospital and on physical examination found increase in blood pressure, namely 185/90 mmHg. On investigation, it was found that the results of blood tests showed an increase in AST: 109 U/L, an increase in ALT: 69 U/L, and an increase in LDH 738 U/L. Hemoglobin, platelets, urea and creatinine are within normal limits. Urinalysis examination revealed proteinuria 500 mg or +2.

Severe pre-eclampsia is preeclampsia with systolic blood pressure 160 mmHg and diastolic blood pressure 110 mmHg accompanied by proteinuria > 5g/24 hours. The diagnosis of severe preeclampsia is found if one or more of the following symptoms are found: systolic blood pressure 160 mmHg and diastolic blood pressure 110 mmHg, proteinuria > 5 g/24 hours, oliguria, namely urine production less than 500cc/24 hours, increased plasma creatinine levels, impaired vision and Cerebral: decreased consciousness, headache, scotomas and blurred vision, epigastric pain or pain in the right upper quadrant of the abdomen (due to stretching of the Glisson capsule), pulmonary edema and cyanosis, severe thrombocytopenia (<100,000 cells/m3), impaired liver function, ie elevated AST and ALT, stunted fetal growth, and the HELLP syndrome (Cunningham, GF, 2010; Perveens et al, 2012). Partial HELLP syndrome is when one or two of the three parameters of the HELLP syndrome are present. According to Tennesse classification, the parameters for HELLP syndrome are Thrombocytopenia (<100,000 cells/m3), Serum LDH > 600,000 IU/L, AST 70 IU/L. In this patient there is an increase in LDH and AST so that it can be diagnosed with partial HELLP Syndrome (POGI, 2016).

In this patient, the risk factors for obesity were found from the results of the physical examination, the weight before pregnancy was 75 kg, height was 157 cm so that the BMI was 30.48 kg/m2 and can be classifed into grade I Obesity. There are many risk factors for the occurrence of preeclampsia such as primigravida, primipaternity, hydatidiform mole, multiple pregnancy, diabetes mellitus, age <20 years or >35 years, history of preeclampsia, kidney disease, and history of hypertension before pregnancy or previous pregnancy, and obesity. In obese patients, there is an imbalance between calorie consumption and energy needs that are stored in the form of fat. Accumulation of fat along the blood vessels causes blood flow to become less smooth so that it has the potential to block blood and result in the supply of oxygen and nutrients to the body being disrupted. This narrowing and blockage by fat spurs the heart to pump blood more vigorously in order to supply the blood needs to the tissues. As a result, blood pressure increases (Perveen et al, 2012; Bilano et al, 2014, Rasmussen et al, 2010).

The therapy given to this patient was the administration of 40% MgSO4 4 grams as an IV bolus, followed by a drip of 40% MgSO4 6 grams in 500cc RL 28 drops/minute, injection of Dexamethasone 12mg/24 hours (for 2 days) and methyldopa 3x500mg, and catheter insertion. foley. Administration of mgSO4 40% 4 Grams as iV bolus followed by drip MgSO4 40% 6 grams in RL 500 cc 28 drops per minute aims to prevent seizures by inhibiting or reducing levels of acetylcholine on nerve fiber stimulation by inhibiting neuromuscular transmission so that competitive inhibition occurs between calcium ions and magnesium ions. The administration of MgSO4 can also reduce the risk of maternal death and it is found that 50% of its administration causes a flushes effect (Jeyabalan et al, 2013; Prawirohardjo, 2011; Uzan et al, 2011).

This patient was given Dexamethasone 12mg/24 hours for 2 days and followed by tapering off aiming for fetal lung maturation, for HELLP syndrome itself can accelerate the improvement of clinical and laboratory symptoms. Improvements in clinical symptoms can be seen from increased urine production and decreased blood pressure (Johnson et al, 2014). Methyldopa is a centrally acting agent and remains the drug of first choice for treating hypertension in pregnancy. It has been the most frequently assessed antihypertensive in randomized trials and has the longest safety track record. Long term use has not been associated with fetal or neonatal problems1 and there are safety data for children exposed in utero.18 Women should be warned of its sedative action and this can limit up titration. The drug may result in an elevation of liver transaminases (in up to 5% of women) or a positive Coomb's test (although haemolytic anemia is uncommon). Methyldopa should be avoided in women with a prior history of depression, because of the increased risk of postnatal depression (Easterling T et al, 2019). The use of a foley catheter in this patient aims to monitor fluid that comes out of the body because it is feared that oliguria will occur (urine production <30 cc/hour in 2-3 hours or <500cc/24 hours) (Cunningham, 2010; Jayebalan, 2013).

Based on the gestational age and the development of severe preeclampsia symptoms during treatment, the attitude towards pregnancy is divided into 2, namely terminating the pregnancy or termination simultaneously with the administration of medical treatment (active management) or by maintaining the pregnancy along with the administration of medication (expectative management). Criteria for terminating pregnancy in preeclampsia can be subdivided into maternal and fetal criteria. Maternal criteria are a severe uncontrollable HT, eclampsia, acute pulmonary edema, retro placental haematoma, oligura (<100 ml in 4 hours) resistant to appropriate fluid expansion, persistent signs of imminent eclampsia (headache or visual disturbances), persistent epigastric pain, HELLP syndrome, new-onset renal failure and a gestation time within the first 24 weeks. The fetal criteria are prolonged and variable fetal heart rate (FHR) decelerations, a short term variability in FHR <3 bpm, a Manning score < or =4 on two separate occasions, severe oligohydramnios, an estimated fetal weight below the 5^{th} percentile beyond the 32^{nd} week of amenorrhea and an inverted diastolic flow in the umbilical artery beyond the 32^{nd} week of amenorrhea. In case of non-severe PE beyond the 36^{th} week of amenorrhea, interruption of the pregnancy must be considered. In this case, the mother found signs of impending eclampsia such as headaches and heartburn, in fetal criteria, the ultrasound results showed that the fetus had Intrauterine Growth Restriction so that active management was taken (Emergency CS) (Jayebalan, 2013).

Indications for conservative treatment are preterm pregnancies <37 weeks without signs of impending eclampsia with good fetal condition. Given treatment t = the same as medical treatment in conservative management. During conservative treatment, the attitude towards

pregnancy is only observation and evaluation, but pregnancy is not terminated. Magnesium sulfate is discontinued when the mother has reached signs of mild preeclampsia, at least within 24 hours. If within 24 hours there is no improvement, this condition is considered a failed expectation and must be terminated (Turner, 2011).

CONCLUSION

The patient was diagnosed with G3P2A0 36 weeks pregnant with Severe Preeclampsia with Partial HELLP Syndrome + IUGR. Active management was chosen because the patient was accompanied by signs of impending eclampsia (severe headaches and heartburn) and the USG of the fetus showed Intrauterine Growth Restriction.

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