


Systemic Lupus Erythematosus (SLE) with Hypertensive Crisis in Pregnancy

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ABSTRACT

Introduction: Although SLE prevalence lacks specific Indonesian data, it predominantly affects women of childbearing age. **Case:** A 24-year-old pregnant woman with a history of SLE experienced worsening shortness of breath, leg swelling, and fatigue since her second month of pregnancy. Hospital admission revealed severe hypertensive crisis, active SLE affecting kidneys, joints, skin, congestive heart failure, and anemia. She underwent rigorous medical treatments and ICU monitoring. **Discussion:** SLE affects multiple organs. Careful management and monitoring are required during pregnancy for maternal and fetal well-being. **Conclusion:** Pregnant women with SLE may encounter various pregnancy-related complications. Effective and comprehensive management is vital to achieve favorable outcomes.

Keywords: Autoimmune disease, pregnancy complications, systemic lupus erythematosus.

ABSTRACT

Pendahuluan: Meskipun belum ada data spesifik prevalensi SLE di Indonesia, penyakit ini lebih umum pada wanita usia subur. **Kasus:** Wanita hamil 24 tahun dengan riwayat SLE mengeluh sesak napas, kaki bengkak, dan kelelahan yang memburuk sejak bulan kedua kehamilannya. Saat masuk rumah sakit didiagnosis krisis hipertensi berat, SLE aktif (ginjal, sendi, kulit), gagal jantung kongestif, dan anemia. Perawatan intensif dilakukan di ICU. **Diskusi:** SLE merupakan penyakit autoimun yang memengaruhi berbagai organ. Manajemen yang hati-hati dan pemantauan diperlukan selama kehamilan untuk kesejahteraan ibu dan janin. **Simpulan:** Wanita hamil dengan SLE berisiko komplikasi kehamilan. Penanganan komprehensif diperlukan untuk hasil yang baik. **Novierta Prima Kusumandaru, Calcarina Fitriani. *Systemic lupus erythematosus* (SLE) dengan Krisis Hipertensi pada Kehamilan.**

Kata Kunci: Penyakit autoimun, komplikasi kehamilan, lupus eritematosus sistemik.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that can affect various organs and tissues in the body.[1] Genetic predisposition environmental and hormonal factors can influence the development and progression of the disease.[2]

The estimated incidence of SLE in the general population is approximately 5.14 cases per 100,000 people per year, ranging from 1.4 to 15.13 cases; approximately 0.40 million new cases of SLE are diagnosed each year.[3] Data from several rheumatology polyclinics in hospitals in Indonesia showed an increase of SLE patient visits: 17.9%-27.2% in 2015, 18.7%-31.5% in 2016, and 30.3%-58% in 2017.[4] SLE mainly affects women of productive age, with a female-to-male ratio of 9 to 1.4.[2,5] Clinical symptoms, based on data from several hospitals in Indonesia, are arthritis (32.9-75%), skin and mucosal disorders (13.2-86.3%), lupus nephritis (10.8-65.5%), fatigue (51.1-58.1%), and fever (39.3-54.9%). The most common laboratory results were positive ANA (98.4%), lymphopenia (75.4%), positive anti-dsDNA (47%), and hemolytic anemia (26.08-34.6%).[4]

Pregnant women with SLE, although in remission, are at risk of several pregnancy complications such as maternal mortality, section cesarean delivery, fetal prematurity, low birth weight (LBW), small neonates, spontaneous abortion, non-viable fetuses, and pre-eclampsia.[3] Women with lupus nephritis have a higher risk of renal and non-renal flares during pregnancy compared to women without renal involvement. Maternal complications include SLE flares (25%), hypertension (16%), active lupus nephritis (16%), and pre-eclampsia (8.4%).[6] Pregnant women with SLE and/or Antiphospholipid Syndrome (APS) should follow the protocols applied in pregnancies with high risk of hypertensive disorders and/or placental insufficiency, adjust the frequency and methods of fetal monitoring according to the condition of the mother and/or fetus.[7,8]

Hypertensive crises are more common in clinically symptomatic SLE patients with APS than in SLE patients without APS. Symptoms related to the cardiovascular system, such as myocarditis, pericardial effusion, heart valve disorders, coronary heart disease, and hypertension, have been observed in many individuals with SLE. Hypertensive crisis or malignant hypertension has been reported in association with autoimmune rheumatoid disease and in patients with antiphospholipid

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antibody syndrome (APS) alone or in association with SLE.[9]

A case of 24-year-old G1P1A0 female with systemic lupus erythematosus (SLE) is reported. Early recognition and intervention are associated with decreased morbidity.

CASE

A 24-year-old primigravida woman at 32 weeks of gestation, came with current complaint of shortness of breath, worsened with activity. The patient was referred from regional hospital to the Obstetrics and Gynecology Department with shortness of breath and swelling in both legs. Shortness of breath was aggravated after four months of pregnancy, and swelling was felt after five months. There were often red spots all over the body and pain in the joints if she was tired. The patient also complained of nausea and vomiting. Fetal movements were felt to be active. Other complaints such as tightening, amniotic leakage, blood mucus discharge, fever, dizziness, heartburn, blurred vision, urination disorder, defecation disorder, vaginal discharge, cough, runny nose, and reddish rash were denied. She had a normal menstrual history and denied any history of contraception nor surgery.

The patient had regular control with an obstetrician (5 times). Since two months of pregnancy, the patient was diagnosed with abnormalities in the kidneys and heart. Transthoracic echocardiography examination showed: 1) MR mild, PR mild, 2) TR mild, 3) Pericard effusion mild, and 4) EF 66%. The diagnosis was Congestive Heart Failure (CHF) Functional Class II.

The patient had a history of two admissions and was co-treated by the Internal Medicine and Cardiology; she was diagnosed with Systemic Lupus Erythematosus (SLE) since 3 years ago; methylprednisolone and azathioprine were given until delivery to prevent lupus flares, worsening of hypertension, and fetal complications such as miscarriage, preterm birth, and neonatal lupus syndrome. Cefixime and nystatin drops were given to prevent bacterial and fungal infections, the patient received furosemide, methyldopa, sildenafil, and ISDN from the cardiology department. These medications were part of a comprehensive treatment plan aimed to managr her severe SLE activity, hypertensive crisis, and associated complications like CHF, hypoalbuminemia, and anemia during pregnancy. Each medication addresses specific aspects of her condition, highlighting the multidisciplinary approach required to manage SLE and its complications during pregnancy. Previous history such as hypertension, diabetes mellitus, allergies, surgery, and use of anesthetic drugs were denied. Family history such as hypertension, diabetes mellitus, allergy, similar complaints, autoimmune disease, and malignancy were denied.

Upon admission, she experienced shortness of breath, joint pain, nausea, and hypertension (171/103 mmHg). Physical examination revealed cardiomegaly, rhonchi, and leg edema. Lab results showed low hemoglobin, hematocrit, platelets, and abnormal counts of eosinophils, lymphocytes, monocytes, and neutrophils. The patient had high blood sugar, low liver enzymes, elevated BUN and creatinine, electrolyte imbalances, and low albumin. Imaging showed pulmonary edema, pneumonia, and pleural effusion.

The diagnosis included hypertensive crisis, severe SLE activity with multiple manifestations, CHF, hypoalbuminemia, and anemia. The treatment plan involves a comprehensive array of medications to address various aspects of their condition. Azathioprine at a dosage of 100 mg daily, furosemide 20 mg iv thrice daily, and ceftriaxone 1 gram iv twice daily to manage underlying systemic lupus erythematosus and potentially associated infections. Methylprednisolone at 125 mg iv daily serves an anti-inflammatory. Aspirin is prescribed at 80 mg pc as antiplatelet agent. Dopamine iv drip 5 mcg/Kg per minute (5 mcg/Kg/min) was given to improve cardiac and renal functions in patients with heart failure16, and calcium lactate tablets at 500 mg thrice daily to fulfill calcium needs.

Despite initial treatment, her condition deteriorated, leading to a series of complications such as increased respiratory distress, hypertension, altered laboratory markers indicating kidney dysfunction, electrolyte imbalances, and decreased hemoglobin levels. This progression need an intensive care, necessitating ventilator support and a tailored regimen of medications, including immunosuppressants, diuretics, antibiotics, and supportive therapies to manage the worsening multi-organ involvement, highlighting the severity of her condition and the complexity of managing her complications, especially during pregnancy.

By the thirteenth day of treatment, the patient's respiratory distress lessened, she was successfully extubated, and her blood pressure stabilized. Each medication is carefully chosen to manage symptoms, prevent complications, and ensure the well-being of both the mother and the fetus. Nicardipine and amlodipine control hypertension, furosemide addresses fluid overload, and paracetamol manages pain and fever safely during pregnancy. Antibiotics like meropenem and levofloxacin combat potential infections due to immunosuppression from SLE and its treatment. Fentanyl provides potent pain relief, aspirin prevents placental thrombosis, and sildenafil manages pulmonary hypertension. Additional supplements like calcium lactate and sodium ferric gluconate cater to increased needs during pregnancy and manage anemia, respectively. Mycophenolate sodium controls SLE activity cautiously, and sucralfate protects against gastrointestinal irritation. This holistic approach underscores the complexity of managing SLE during pregnancy, emphasizing immediate concerns, infection prevention, pain management, and mitigating risks to both maternal and fetal health.

DISCUSSION

SLE is a complex chronic autoimmune disease affecting various body organs and tissues. Genetic predisposition, environment, and hormonal factors can influence the development and progression of this disease.[2] Approximately 0.40 million new Systemic Lupus Erythematosus (SLE) cases are diagnosed each year. The estimated incidence of SLE in the general population is approximately 5.14 cases per 100,000 people per year, ranging between 1.4 to 15.13 cases.[3]

Several genetic, immunological, endocrine, and environmental factors play a role in the etiopathogenesis of SLE.[5] In genetically susceptible individuals, immune tolerance breaks down when exposed to environmental factors such as UVB radiation, infections, and toxins, which trigger autoimmune responses.

Women who have recently been diagnosed


with early-stage SLE or are experiencing active disease should consider delaying pregnancy and using reliable birth control methods. It is advisable to reassess their medications, favoring immunosuppressive drugs such as hydroxychloroquine (HCQ) and/or azathioprine, which are considered safe options during pregnancy.[10]

Clinical symptoms of SLE involve multi-organ systems that are constitutional manifestations (fatigue, fever, weight loss, lymphadenopathy), mucocutaneous (malar rash, widespread photosensitive rash, discoid rash), musculoskeletal (arthritis and arthralgia), renal (lupus nephritis), gastrointestinal and hepatic (esophageal dysmotility, mesenteric vasculitis, lupus enteritis, peritonitis, and ascites), cardiovascular (pericarditis, myocarditis, and heart failure), pulmonary (shortness of breath, pleural effusion, pulmonary embolism), neuropsychiatric (headache and seizures), hematological (anemia and thrombocytopenia), and ocular (keratitis, episcleritis).[11]

Pregnant women with SLE are at risk of pregnancy complications such as maternal death, cesarean delivery, fetal prematurity, low birth weight (LBW), small neonates, spontaneous abortion, non-viable fetuses, and pre-eclampsia.[4] SLE usually gets worse during pregnancy, primarily if the disease was not controlled in the six months before pregnancy. Lupus nephritis can be challenging to differentiate from pre-eclampsia. Some clinical and laboratory features (low complement, positive Anti-ds-DNA antibodies, normal serum uric acid levels, and active urine sediment) can help diagnosis.[5,6]

The European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR) collaborated to establish and publish updated Systemic Lupus Erythematosus (SLE) classification criteria in 2019.[12] These criteria consist of various clinical and immunological parameters, including mucocutaneous, musculoskeletal, renal, neurological, hematological, and immunological manifestations, alongside specific laboratory findings. The criteria provide a scoring system, requiring at least 10 points from a combination of clinical and immunological criteria to diagnose SLE.[12] Additionally, the presence of ANA-IF (Antinuclear Antibody-Immunofluorescence) at a titer of 1:80 or higher, or its equivalent in other testing methods, is considered a significant factor in the EULAR criteria.[13] This updated criteria set has shown a validated sensitivity of 96.12% and specificity of 93.38%, aiding clinicians to accurately diagnose and classify systemic lupus erythematosus based on a standardized and comprehensive assessment of various disease manifestations and laboratory findings.[2]

This case is a 24-year-old primigravida at 32 weeks of gestation diagnosed with SLE. This patient was subsequently diagnosed with hypertensive crisis, severe activity of SLE with manifestations of nephritis, arthritis, mucocutaneous, CHF FC II, primigravida at 32 weeks, hypoalbuminemia, and normocytic normochromic anemia. This patient's diagnosis of severe systemic lupus erythematosus (SLE) was based on a constellation of clinical features including nephritis, arthritis, and mucocutaneous manifestations, alongside complications such as congestive heart failure (CHF) at Functional Class II. The diagnosis was established considering the patient's history of systemic lupus erythematosus over the past three years, along with active symptoms during pregnancy.

Based on the IRA classification, this patient's SLE has presented with a spectrum of clinical manifestations including ascites, rash affecting more than 18% body surface area, platelets below 20,000/mm^3, severe pleurisy with pleural effusion, Diffuse Alveolar Hemorrhage (DAH), severe pericarditis with significant pericardial effusion, psychosis, cerebritis, and a high SLEDAI score of ≥12 or MEX-SLEDAI ≥10.[2,14] Lupus nephritis, commonly seen in SLE patients, results from a type-3 hypersensitivity reaction, leading to immune complex deposition in the renal glomerulus. The formation of anti-double-stranded DNA (anti-dsDNA) antibodies plays a crucial role in this process, triggering an inflammatory response and subsequent renal manifestations.[15]

Hypertensive Crisis (HC) emerged as a significant concern in this patient despite no prior history of hypertension. HC, characterized by a substantial increase in blood pressure, can induce ischemic retinal injury, indicating grade III or IV hypertensive retinopathy.[9] This condition also potentially involves renal abnormalities such as arteriolar fibrinoid necrosis, onionskin lesions, and hematological disorders like microangiopathic hemolytic anemia. Cardiovascular symptoms linked with SLE encompass a broad spectrum of manifestations, including pericarditis, impaired left ventricular function, early coronary atherosclerosis, heart valve disorders, and systemic arterial hypertension. Hypertension poses a considerable risk in SLE patients, potentially contributing to premature mortality due to atherosclerotic events or renal failure, with prevalence ranging between 14% to 58.1% across different ethnic population.

Genetic predisposition may play a crucial role in developing congestive heart failure (CHF) in individuals with SLE, with higher risks noted in both European and East Asian populations.[4] Lupus nephritis flares during pregnancy can often mimic pre-eclampsia, leading to challenges in diagnosis due to overlapping clinical and laboratory features. Management strategies for pregnant women with SLE involve considering medications such as hydroxychloroquine, glucocorticoids, azathioprine, and calcineurin inhibitors to control disease activity and prevent flares. Intravenous immunoglobulin, plasmapheresis, and high-dose glucocorticoids could be considered for moderate to severe flare-ups, whereas caution is warranted regarding the use of cyclophosphamide during the first trimester due to potential miscarriage risks.[7,16]

In SLE with hypertensive crisis in pregnancy, the treatment is a critical. The management of SLE during pregnancy involves a multidisciplinary approach, close monitoring, and, in some cases, termination of pregnancy at the appropriate time.[17,18] Additionally, the use of glucocorticoids, mycophenolate mofetil, hydroxychloroquine, and granulocyte colony-stimulating factor has been reported in the treatment of SLE during pregnancy.[19,20] It is important to note that none of the medications is absolutely safe during pregnancy, and their use should be carefully considered, especially in the presence of active lupus nephritis and uncontrolled hypertension.[21] Hydroxychloroquine (HCQ) has been studied and shown to potentially reduce the risk of preeclampsia, pregnancy hypertension, and prematurity in SLE patients.[18,22,23] However, the management of SLE during pregnancy should

be individualized, and the potential benefits and risks of treatment options should be carefully evaluated individually.

The patient's treatment plan encompassed a combination of medications targeting SLE and its complications, involving immunosuppressants, diuretics, antiplatelet agents, and supplements. Despite initial improvement, the patient faced complications necessitating intensive care, including ventilator support and a diverse regimen of medications. Subsequently, by the thirteenth day of treatment, her respiratory distress decreased, she was extubated successfully, and her blood pressure stabilized, while the prescribed medications were continued to address her complex clinical conditions, acute respiratory distress syndrome, SLE activity alongside postpartum complications.

CONCLUSION

Pregnancy with Systemic Lupus Erythematosus (SLE) poses complex challenges. Vigilant care and tailored management are crucial, considering complications like hypertensive crises, multi-organ SLE activity, and elevated pregnancy risks. Caution with immunosuppressants like hydroxychloroquine is vital. Early recognition and precise interventions are essential for improved maternal and fetal outcomes.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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