Diagnostic and Management Challenges of Systemic Lupus Erythematosus in Pregnancy Complicated with Severe Preeclampsia and Intrauterine Growth Restriction: A Case Report

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Abstract

Introduction: Systemic lupus erythematosus (SLE) is a chronic systemic autoimmune disease more common in women than men. The risk of lupus flare increases during pregnancy. This case report describes the diagnostic and management challenges of SLE in pregnancy.

Case Illustration: This case report describes a 27-year-old female, G3P1A1, 27 weeks of pregnancy, who presented with a six-hour history of headache, epigastric pain, and irregular uterine contractions. The patient has a poor obstetric history, with a miscarriage in her first pregnancy and an intrauterine fetal death (IUFD) in her second pregnancy. Ultrasonography showed an estimated fetal weight (EFW) of 878 grams. The laboratory test results revealed elevated levels with ANA of 140.2 units, anti-dsDNA of 1094 IU/mL, positive direct and indirect Coombs tests, and 1000 mg/dL urine protein.

Conclusion: The diagnosis of SLE is established when a group of symptoms and signs are found according to the SLE Risk Probability Index criteria or the criteria for SLE in The Assessment using the European League Against Rheumatism/American College of Rheumatology. Early diagnosis of SLE in women is expected to prevent its impact on pregnancy. Management of SLE during pregnancy includes the use of hydroxychloroquine, azathioprine, steroid therapy, and addressing any complications that have occurred.

Keywords: Pregnancy, Preeclampsia, Systemic lupus erythematosus

Tantangan Diagnosis dan Tatalaksana Lupus Eritematosus Sistemik pada Kehamilan yang Disertai Preeklampsia Berat dan Restriksi Pertumbuhan Intrauterin: Sebuah Laporan Kasus

Abstrak

Pendahuluan: *Systemic lupus erythematosus* (SLE) adalah penyakit autoimun sistemik kronis yang lebih sering terjadi pada perempuan dibandingkan dengan laki-laki. Risiko lupus flare meningkat selama kehamilan. Laporan kasus ini bertujuan untuk menjelaskan tantangan diagnostik dan tatalaksana SLE pada kehamilan.

Laporan Kasus: Laporan kasus ini menggambarkan seorang perempuan berusia 27 tahun, G3P1A1, usia kehamilan 27 minggu yang datang dengan keluhan nyeri kepala, nyeri epigastrium, dan kontraksi rahim tidak teratur selama enam jam. Pasien memiliki riwayat obstetri yang kurang baik, dengan keguguran pada kehamilan pertama dan kematian janin dalam kandungan (IUFD) pada kehamilan kedua. Pemeriksaan ultrasonografi menunjukkan estimasi berat janin (EFW) sebesar 878 gram. Hasil pemeriksaan laboratorium menunjukkan peningkatan ANA sebesar 140,2 unit, Anti-dsDNA sebesar 1094 IU/mL, tes Coombs langsung dan tidak langsung yang positif, serta protein urin sebesar 1000 mg/dL.

Kesimpulan: Diagnosis SLE ditegakkan apabila ditemukan kumpulan gejala dan tanda sesuai *SLE Risk Probability Index* (SLERPI) atau kriteria SLE pada *The assessment using the European League Against Rheumatism/American College of Rheumatology* (EULAR/ACR). Penegakan dini SLE pada perempuan diharapkan dapat mencegah dampaknya pada kehamilan. Tatalaksana SLE selama kehamilan meliputi pemberian hydroxychloroquine, azathioprine, terapi steroid, serta penanganan komplikasi yang telah terjadi.

Kata kunci: Kehamilan, Preeklamsia, Sistemik lupus eritematosus

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Introduction

Systemic Lupus Erythematosus (SLE) is a complex autoimmune condition characterized by the immune system's aberrant attack on the body's healthy tissues, leading to a wide range of potential complications.[1] When SLE coexists with pregnancy, it can further exacerbate the intrinsic physiological and immunological changes, often resulting in poorer maternal and fetal outcomes.[2]

There are no reports on the incidence of SLE in pregnancy; however, SLE is more common in women than in men,[3] with an increased risk of lupus flare during pregnancy.[4] Existing literature has associated pregnancy in women with SLE with elevated risks of lupus flare, preeclampsia, thrombosis, hypothyroidism, miscarriage, intrauterine growth restriction (IUGR), neonatal lupus, and even fetal mortality.[5] Moreover, the management of SLE during gestation can be particularly challenging, as certain medications used to control the disease may not be safe for the developing fetus.[6] Healthcare providers must, therefore, carefully balance the need to mitigate the mother's SLE symptoms with the potential hazards to the unborn child.

Recent research has also highlighted the potential for placental damage in pregnancies complicated by SLE.[7] This placental compromise can further jeopardize fetal development and well-being. Additionally, SLE during pregnancy was associated with higher rates of maternal and neonatal complications, underscoring the importance of effective management strategies.[8] This case report aims to illustrate the diagnostic and management complexities that can arise when caring for a pregnant patient with pre-existing SLE. By examining a specific patient's clinical course and outcomes, we hope to provide insights that can inform the care of other women facing similar circumstances.

Case Report

This case report describes a 27-year-old female, gravida 3, para 1, abortus 1 (G3P1A1), at 27 weeks of gestation, who presented with a six-hour history of headache and irregular uterine contractions. She denied symptoms such as shortness of breath, fever, or fluid discharge from the birth canal but reported experiencing epigastric pain. The patient has a poor obstetric history, with a miscarriage in her first pregnancy and an intrauterine fetal death (IUFD) in her second pregnancy. She had no history of hypertension, diabetes, thyroid disease, or previously diagnosed autoimmune disease. Upon admission, the patient's vital signs indicated hypertension with a blood pressure of 170/100 mmHg, a pulse rate of 67 bpm, respiratory rate of 20 bpm, and oxygen saturation at 96% with 3 lpm nasal cannula oxygen. Abdominal examination revealed a single fetus in the longitudinal position, with a fetal heart rate of 162 bpm. The patient exhibited mild edema in her lower extremities. Other general examination findings were within normal limits, and no oral ulcers, arthritis, malar rash, alopecia, or other skin disorders were detected. The patient had been hospitalized previously for conservative management of preeclampsia, receiving intravenous magnesium sulfate (MgSO4) 40% 4g, diluted with 10 ccs of aquades, administered as an IV bolus slowly over 15 minutes, followed by MgSO4 40% 6g with Ringer lactate (RL) 500cc drips over 6 hours, at a rate of 1g/hour for 24 hours. Intramuscular dexamethasone 6 mg twice daily for 2 days. The patient was also prescribed oral nifedipine 10 mg three times a day, folic acid once daily, and Aspilet 100 mg once daily. Despite this, her blood pressure remained elevated. Further ultrasonography showed a fetal heart rate (FHR) of 153 beats per minute (Fig 1A), adequate amniotic fluid (SDP 3.68), an estimated fetal weight (EFW) of 878 grams,

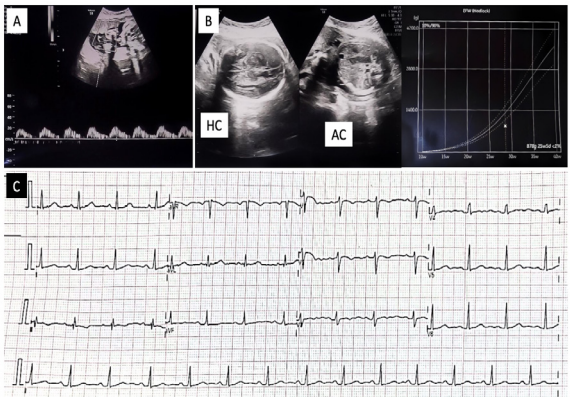

Figure 1 Ultrasound and electrocardiogram (ECG) examination. Fetal heart rate (FHR) of 153 bpm (A) and estimated fetal weight (EFW) of 878 grams based on head circumference (HC) and abdominal circumference (AC) (B). Normal sinus rhythm on ECG (C)

Table 1 Laboratory Examination Results

Laboratory Examination	Result	Unit	Normal Value
Hemoglobin	11.7	g/dL	11.7-15.5
Hematocrit	35	%	32-62
Eritrosit	3.92	10^6/uL	4.4-5.9
Leukosit	9.6	10^3/uL	3.6-11
Trombosit	191	10^3/uL	150-400
			Diabetes >=6.5
			Pre-Diabetes 5.7-6.4
HBA1c	4.8	%	Normal <5.7
SGOT	25	U/L	15-34
SGPT	19	U/L	15-60
Ureum	32	mg/dL	10-50
Creatinin	1.2	mg/dL	0.6-1.2

and normal flow in the umbilical artery. From the graph, a diagnosis of Category 1 IUGR can be made (Figure 1B). A cardiotocography examination was not performed.

The patient was transferred to Dr. Kariadi General Hospital in Semarang for further evaluation. The laboratory test results revealed elevated levels with ANA of 140.2 units, Anti-dsDNA of 1094 IU/mL, positive direct and indirect Coombs tests, and urine protein of 1000 mg/dL, resulting in the SLE Risk Probability Index (SLERPI) score of 10. The assessment using the European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) criteria also yielded a score of 10. Additional laboratory results are presented in Table 1. The Doppler ultrasound results showed a resistive index of 0.72 (percentile 50-95) and a pulsatility index of 1.27 (percentile 50-95). The patient is diagnosed with SLE complicated with severe preeclampsia and IUGR. Treatment was adjusted accordingly, with the addition of hydroxychloroquine sulfate 200 mg daily, azathioprine 50 mg daily, methylprednisolone 8 mg twice daily, enoxaparin 40 mg daily,

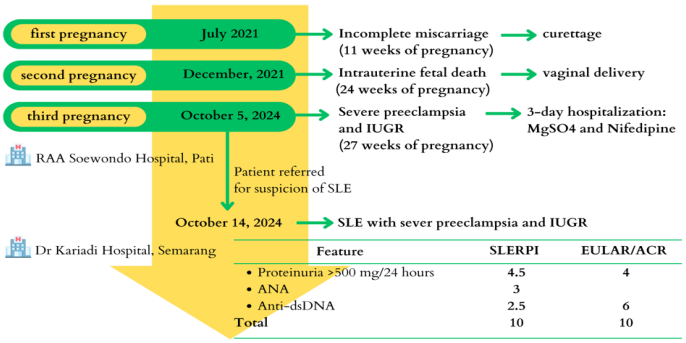

Figure 2 Timeline of the patient's diagnosis and management

nifedipine 30 mg once daily, folic acid once daily, ferrous sulfate twice daily, vitamin C 50 mg once daily, vitamin D 5000 IU once daily, and asetosal 100 mg (low-dose aspirin) once daily. The patient's diet was high in calories and low in protein. All medications were taken until delivery. This therapy aimed to manage both her autoimmune condition and reduce the risk of thrombotic complications associated with SLE during pregnancy.

The patient was admitted for 4 days, with a discharge blood pressure of 153/99 mmHg. The patient is scheduled for weekly follow-up appointments with the obstetrician and the internist.

Discussion

In this case, the woman experienced complications in all three pregnancies, including abortion, IUFD, and currently severe preeclampsia with IUGR. It is crucial to identify SLE in women before marriage to determine their readiness for pregnancy and prevent increased morbidity in pregnant women.[9,10] SLE is a chronic systemic autoimmune disease involving innate and adaptive immune responses, where the interaction between genes and environmental factors causes damage to various body tissues due to autoantibodies and immune complex deposition.[11] The diagnosis of SLE using the SLERPI has a sensitivity of 94.2% and a specificity of 94.4%.[12] This patient has a SLERPI score of 10, enabling us to establish the diagnosis of SLE. The assessment using the EULAR/ACR criteria resulted in a score of 10.[11] Additionally, the diagnosis of systemic lupus erythematosus (SLE) could also be confirmed using the Systemic Lupus International Collaborating Clinics (SLICC) 2012 criteria.

SLE disease severity and progression can vary significantly among patients.[11] Disease activity in SLE can be assessed using either the SLE Disease Activity Score (SLE-DAS) or the Easy British Isles Lupus Assessment Group (Easy-BILAG) scoring systems.[13] For SLE patients planning pregnancy, it is recommended to wait until six months after achieving remission or maintaining stable low disease activity.[14] Previous research has demonstrated that SLE during pregnancy significantly increases the risk of adverse outcomes, including low birth weight (P= 0.003), preeclampsia (P= 0.012), and IUFD (P= 0.036).[15] Therefore, it is essential for women with SLE to undergo proper medical management before conception, throughout pregnancy, and during the postpartum period.

Hydroxychloroquine (HCQ) at 5mg/kg/day is recommended for all patients, including pregnant women, unless contraindicated.[11] Studies have shown that HCQ administration reduces the risk of high lupus activity during pregnancy and the incidence of preeclampsia

in SLE patients.[16] Furthermore, HCQ treatment has demonstrated effectiveness in reducing the occurrence of neonatal lupus and congenital heart block.[17] Moderate to severe stages of SLE are indications for immunosuppressive therapy, including methotrexate and azathioprine.[11] Methotrexate is associated with a high teratogenic risk, while azathioprine is more commonly used in SLE patients with hypertension or renal disease.[18] The use of azathioprine does not have teratogenic effects and is not associated with low birth weight.[19]

Preeclampsia is a common complication in pregnancies complicated by SLE.[15] Due to similar manifestations between preeclampsia and lupus nephritis (LN) in SLE patients, these conditions can coexist, making diagnosis challenging.[20] According to the 2021 Kidney Disease: Improving Global Outcomes (KDIGO) guidelines, steroid therapy is recommended for class I/II LN, while the 2019 EULAR/ARC guidelines recommend steroid treatment for class III/IV LN.[21] Additionally, low-dose aspirin can serve as an adjunctive therapy to prevent preeclampsia in SLE patients.[22] The therapeutic target for LN is to achieve proteinuria levels less than 0.5-0.7 g/24 hours within 12 months, along with normalization or stabilization of the glomerular filtration rate.[21] The initial management of severe preeclampsia involves the administration of magnesium sulfate (MgSO4), corticosteroids, and antihypertensive agents such as labetalol, nifedipine, and methyldopa. Preeclampsia patients are advised to practice bed rest. The recommended diet includes high-fiber foods, low-fat options, and limiting sodium intake to less than 2.4 grams daily. In the absence of multi-organ dysfunction or HELLP syndrome, delivery is recommended after 34 weeks of gestation. [23]

Early-onset IUGR is associated with severe preeclampsia in 60% of cases, as it results from impaired blood flow rich in nutrients and oxygen in the umbilical vein. [23] Inelastic blood vessels reduce uteroplacental blood flow, leading to IUGR.[24] Therefore, we believe that appropriate preeclampsia treatment, sufficient vitamins, and nutritional support can improve fetal weight. A high-calorie and low-protein diet in women at high risk of nutritional deficiencies can improve fetal growth.[23] Low vitamin D levels are associated with IUGR,[25] but supplement trials showing benefit are lacking.[23]

This study's limitation is that we could not conduct further follow-up as the patient was referred to a different city. Additionally, due to time constraints, we could not report on the outcome up to delivery. Delivery planning is based on Doppler findings, fetal condition, and gestational age. Corticosteroids are administered to promote lung maturation in patients scheduled for delivery before 34 weeks of gestation. Magnesium sulfate is used for neuroprotection in cases where delivery occurs before 32 weeks of gestation.[23] We hope this study can serve as a foundation for future research of a more advanced nature.

Conclusion

Systemic lupus erythematosus during pregnancy is a condition that warrants careful monitoring. The diagnosis of SLE can be established using the SLERPI or EULAR/ACR criteria. Early diagnosis is essential to prevent increased maternal and fetal morbidity and mortality. Pregnant patients with SLE are at heightened risk for complications, including preeclampsia, miscarriage, IUGR, and IUFD. Immunosuppressive therapies, such as hydroxychloroquine, azathioprine, and corticosteroids, are considered safe and effective for use during pregnancy.

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