CASE REPORT

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A challenging strategy toward severe maternal outcome adversed from systemic lupus erythematosus and nephrotic syndrome in pregnancy: a case report

Ida Bagus Gde Fajar Manuaba[1], Putu Doster Mahayasa[2], Nyoman Gede Budiana[3], I Gusti Ngurah Agung Trisnu Kamajaya[4*], Samuel Albert Andrian[4]

[1]Obstetric and Gynecologic Departments, Prof IGNG Ngoerah Hospital/ Faculty of Medicine, Universitas Udayana, Bali, Indonesia;
[2]Fertility Endocrinology and Reproduction Consultant, Obstetric and Gynecologic Departments, Prof IGNG Ngoerah Hospital/ Faculty of Medicine, Universitas Udayana, Bali, Indonesia;
[3]Oncology Gynecology Consultant, Obstetric and Gynecologic Departments, Prof IGNG Ngoerah Hospital/ Faculty of Medicine, Universitas Udayana, Bali, Indonesia;
[4]Obstetric and Gynecologic Resident, Faculty of Medicine, Universitas Udayana, Bali, Indonesia.

*Correspondence:
I Gusti Ngurah Agung Trisnu Kamajaya;
Obstetric and Gynecologic Resident, Faculty of Medicine, Universitas Udayana, Bali, Indonesia;
kamajayatrk@gmail.com

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ABSTRACT

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disorder that affects multiple organ systems, characterized by the production of autoantibodies and a wide range of symptoms resulting from damage to vital organs. Renal involvement is observed in approximately 40% of SLE patients and can present as various forms of glomerulonephritis, including membranous lupus nephritis, diffuse proliferative glomerulonephritis, and minimal-change nephropathy (MCN), particularly in cases associated with nephrotic syndrome. This case report highlights the therapeutic challenges in managing women with severe SLE and nephrotic syndrome during pregnancy and the postpartum period.

Case presentation: A 21-year-old woman at 37 weeks of gestation presented with a history of nephrotic syndrome secondary to severe SLE. She was diagnosed with nephrotic syndrome at 30 weeks of pregnancy, with differential considerations including pregnancy complications and severe SLE activity (ACR/EULAR score 10). Additional diagnoses included lupus nephritis, stage II hypertension, mild anemia (hemoglobin 8.9 g/dL), hypoalbuminemia (1.5 g/dL), hypercholesterolemia, anasarca edema, oligohydramnios, and a non-reactive non-stress test (NST). An emergency cesarean section was performed successfully, after which the patient was admitted to the high-care unit for close postoperative monitoring. Post-surgery, she received multidisciplinary management involving an intensivist and a nephrologist.

Conclusion: This study explores the interplay between SLE and nephrotic syndrome, focusing on their impact on maternal and fetal health during pregnancy. It highlights the importance of a multidisciplinary approach in managing these conditions to mitigate the risk of severe maternal and fetal complications.

Keywords: maternal and fetal outcome, nephrotic syndrome, systemic lupus erythematosus.
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INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that affects multiple organ systems, characterized by the production of autoantibodies and a wide spectrum of symptoms resulting from organ damage. Its prevalence among women ranges from 164 to 406 per 100,000 individuals, with the majority of cases occurring in women of childbearing age.[1] The relationship between pregnancy and SLE remains complex and not fully understood. While some studies suggest that pregnant women with SLE can achieve relatively favorable outcomes, others indicate a higher prevalence of adverse pregnancy outcomes compared to healthy individuals. The incidence of nephrotic syndrome during pregnancy is estimated to be 0.012–0.025% of all pregnancy cases. Additionally, renal involvement is observed in approximately 40% of SLE patients, presenting in various forms of glomerulonephritis, including membranous lupus nephritis, diffuse proliferative glomerulonephritis, and minimal-change nephropathy (MCN).[2] Pregnant women with SLE complicated by nephrotic syndrome are considered high-risk due to the increased likelihood of maternal and fetal morbidity and mortality. This case report presents a 37-week pregnant woman with SLE, further exacerbated by nephrotic syndrome. It explores strategies to address the challenges associated with managing severe SLE during pregnancy to improve maternal and fetal outcomes.

CASE REPORT

A 21-year-old woman at 37 weeks of gestation, with a history of nephrotic syndrome secondary to a primary disease and differential diagnosis of pregnancy complications, was referred to the obstetrics and gynecology department due to decreased fetal movements since the previous day. Nephrotic syndrome was diagnosed at 30 weeks of gestation. The patient denied a history of intermittent abdominal pain or vaginal discharge but reported swelling in her face and

Table 1. Laboratory examination of the patient

	20-03-2024	09-04-2024 (Hospitalized)	10-04-2024 (First day post-surgery)	15-04-2024 (One day before discharge)
HGB (g/dL)	**9.30**	**8.90**	**9.10**	
RBC (x10^6/µL)	**2.98**	**2.87**	**2.95**	
PLT (x10^3/µL)	343.00	376.00	373.00	
MCHC (g/dL)	33.90	34.80	34.70	
MCH (pg/cell)	31.20	31.00	30.80	
MCV (fL)	91.90	89.20	88.80	
HCT (%)	**27.40**	**25.60**	**26.20**	
WBC (x10^3/µL)	**11.81**	9.59	**13.80**	
LY# (x10^3/µL)	2.19	2.11	1.24	
NE# (x10^3/µL)	**9.08**	6.93	**12.05**	
HbA1C (%)		4.8		
Immunology Test				
HBsAg	Non-Reactive			
Anti HCV	Non-Reactive			
Ana IF		**Pattern: Fine speckled, titer 1:100.**		
Coombs test		Negative		
Liver Function				
AST/SGOT (µ/L)	13.00	16.00		
ALT/SGPT (U/L)	12.00	7.00		
Albumin (g/dL)	**1.50**	**1.40**	**1.60**	
Lipid Profile				
Total Cholesterol (mg/dL)	**568**			
LDL Cholesterol (mg/dL)	**322**			
HDL Cholesterol (mg/dL)	**86**			
Renal Function				
Triglyceride (mg/dL)	**644**			
BUN (mg/dL)	17.7	**5.9**	**6.3**	18.6
Creatinine (mg/dL)	1.10	**1.28**	**1.27**	0.87
e-GFR (mL/min/1.73m^2)	**71.71**	**59.70**	**60.27**	95.22
Urine vol / 24 hour (ml)	300			
Esbach Protein	7			
Loss Protein (Esbach Protein)	2.10			
Total Protein Micro (Urine)	**657.40**		**327.50**	**881.90**
Protein Creatinine Ratio	**13.15**		**13.88**	**30.84**
Urine Creatinine	**50.0**		**23.6**	**28.6**
Electrolyte				
Potassium (mmol/L)		**3.13**		
Sodium (mEq/L)		141		
Urinalysis				
Specific gravity	1.015			
Turbidity	Clear			
pH	6.00			
Leucocyte	Positive			
Nitrite	Negative			
Protein	(4+)			
Glucose	Negative			
Color	Yellow			
Erythrocyte sediment	0			
Bacteria	**2146.30**			
Cylinder	0.14			
Ketones	Negative			

	20-03-2024	09-04-2024 (Hospitalized)	10-04-2024 (First day post-surgery)	15-04-2024 (One day before discharge)
Blood	Negative			
Urobilinogen	Normal			
Bilirubin	Negative			
Leucocyte sediment	20			
Epithelial cell sediment	4			

Note: Purple text indicates below normal range. Red text indicates above normal range.

legs, which began seven months earlier. Initially localized to the legs, the swelling progressed to involve the face over the past month. She also experienced dyspnea upon lying down and after prolonged walking. The patient denied joint pain, fever, or intermittent abdominal pain, but reported hair loss starting seven months prior. Urine output was reduced to approximately 300 mL per day. This was her second pregnancy; the first, three years prior, resulted in a healthy infant weighing 2800 g delivered vaginally.

On physical examination, the patient's blood pressure was 124/100 mmHg, heart rate 82 beats per minute, respiratory rate 18 breaths per minute, and body temperature 36.6°C. Her weight increased from 49 kg pre-pregnancy to 60 kg, with a body mass index of 19.6 kg/m². Periorbital edema and bilateral pedal edema were observed. Fundal height measured two fingers above the processus xiphoid, and fetal heart rate was 148 beats per minute. A non-stress test was non-reactive. Fetal ultrasound revealed no abnormalities, but abdominal ultrasound showed signs of nephritis with bilateral moderate hydronephrosis. Laboratory results are presented in Table 1, with ANA-IF showing a fine speckled pattern and a titer of 1:100.

The patient was diagnosed with G2P1001 at 37 weeks and 1 day of gestation, with nephrotic syndrome attributed to a primary disease and differential diagnoses including pregnancy complications, severe systemic lupus erythematosus (SLE) activity (ACR EULAR score 10), lupus nephritis, stage II hypertension, mild anemia (Hb 8.9 g/dL), hypoalbuminemia (1.5 g/dL), hypercholesterolemia, anasarca edema, oligohydramnios, and a non-reactive non-stress test (NST). An emergency cesarean section was performed successfully, delivering a male infant weighing 2160 g with an APGAR score of 9/10 and no congenital abnormalities. The mother was admitted to the high-care unit for close postoperative monitoring and managed by a multidisciplinary team, including an intensivist and a nephrologist.

The patient's treatment included candesartan 8 mg once daily orally, potassium chloride 600 mg twice daily orally, simvastatin 20 mg once daily orally, furosemide 20 mg twice daily intravenously, spironolactone 25 mg each morning, methylprednisolone pulse therapy (500 mg in 250 mL normal saline) for 3 days, and hydroxychloroquine 200 mg once daily orally. Mycophenolate mofetil (MMF), mycophenolic acid (MMA), and cyclophosphamide were not administered due to breastfeeding. Fluid intake was restricted to 1–1.5 L/day, and dietary modifications included a very low-fat diet (<20% of total daily calories) and protein intake of 0.8 g/kg body weight/day (~7 g). Albumin supplementation was provided for 3 days. Plans were made for Provider Initiated Testing and Counseling (PITC) and renal biopsy once the patient's condition stabilized. The patient showed continuous improvement and was discharged for outpatient care after 6 days.

DISCUSSION

Systemic lupus erythematosus (SLE) is an autoimmune disease that affects multiple organ systems and is more prevalent in women. As SLE often begins at a young age and survival rates have improved, pregnancy has become more common in affected individuals. Despite this, pregnancy in women with SLE remains high-risk, with an increased likelihood of maternal and fetal complications, alongside more significant healthcare needs and costs. Achieving optimal outcomes requires multidisciplinary collaboration and close monitoring.[3]

Research has shown that active SLE at the time of conception significantly raises the risk of disease flares during pregnancy. In one study of 155 pregnant individuals with lupus, those with active disease at conception faced a higher incidence of renal and hematologic complications. Within this group, 6.1% experienced maternal mortality, and 15.9% progressed to organ failure. Furthermore, low complement protein levels and the presence of anti-double-stranded DNA antibodies at conception were identified as factors contributing to the increased likelihood of disease flares.[4,5]

Idiopathic nephrotic syndrome (iNS) or marked proteinuria in SLE is frequently associated with immune deposits along the glomerular capillary walls, often accompanied by endocapillary proliferation or necrosis. Nevertheless, some reports document instances where lupus patients present with nephrotic syndrome despite the absence of immune deposits in the capillary walls or cellular proliferation.[2] SLE has been strongly linked to idiopathic nephrotic syndrome (iNS), with studies suggesting that SLE may serve as a triggering factor for iNS. Renal involvement is observed in approximately 40% of SLE patients and can present as various forms of glomerulonephritis, including membranous lupus nephritis, diffuse proliferative glomerulonephritis, and minimal-change nephropathy (MCN). This pathology often involves circulating immune complexes depositing in the glomeruli or forming in situ when autoantibodies target intrinsic glomerular antigens (e.g., annexin 2) or antigens released during apoptosis. Inadequate clearance of apoptotic debris, such as chromatin, may also contribute. These intraglomerular immune complexes activate complement pathways and bind to leukocyte Fc receptors, leading to inflammation and kidney damage. In the present case, a renal biopsy could not be

performed due to the patient's unstable condition, preventing confirmation of immune deposits in the glomerular capillary wall.

Previous research has shown that individuals with systemic lupus erythematosus (SLE) experience higher rates of preterm birth and cesarean delivery compared to the general population. SLE has long been associated with an increased risk of pregnancy complications, including preterm delivery. Factors contributing to preterm birth in SLE include active disease during pregnancy, the presence of anticardiolipin (aCL) antibodies, hypertension, and the use of prednisone before or during pregnancy. Smaller studies have estimated that 40% to 75% of preterm births in SLE cases are medically indicated.[6] On the other hand, complications of idiopathic nephrotic syndrome during pregnancy may include maternal hyperlipidemia, hypercoagulability, increased susceptibility to infections, progression to end-stage renal failure, and adverse fetal outcomes.[7] In this case, the patient underwent an emergency cesarean section due to both maternal and fetal indications. From the maternal perspective, there was progressive worsening of swelling and kidney function. From the fetal perspective, decreased fetal movement and a non-reactive NST (non-stress test) were observed. These factors prompted clinicians to proceed with an emergency cesarean section.

Commonly used immunosuppressive agents such as cyclophosphamide, methotrexate, and mycophenolate carry teratogenic risks and should ideally be discontinued prior to conception. Safe alternatives for immunosuppression during pregnancy include azathioprine and calcineurin inhibitors like tacrolimus and cyclosporine, which have demonstrated safety and efficacy in numerous studies. However, one study indicated a potential link between maternal azathioprine use and late developmental delays in offspring, though further research is required to confirm this. Higher doses of azathioprine may increase the risk of fetal cytopenia and immune suppression, and it is generally recommended to limit the dosage to no more than 2 mg/kg/day. While limited data suggest that unintentional exposure to leflunomide may not pose a significant risk when followed by cholestyramine washout, more research is needed. Maintaining hydroxychloroquine treatment during pregnancy has been shown to reduce the risk of disease flares both during pregnancy and postpartum. Additionally, a study involving 316 pregnancies in women with lupus found that hydroxychloroquine use was associated with a lower risk of preeclampsia.[8,9] In this case, we did not use cyclophosphamide because we considered that the mother wanted to breastfeed. Besides, we use hydroxychloroquine and methylprednisolone as the mainstay agents to suppress the immune.

CONCLUSION

Severe maternal outcomes associated with SLE and nephrotic syndrome during pregnancy are rare and highly complex, placing such cases in the high-risk category due to substantially elevated risks of maternal and fetal morbidity and mortality. Strict adherence to treatment protocols is essential, as the prognosis for pregnancies complicated by active SLE and nephrotic syndrome is generally unfavorable.

PATIENT'S INFORMED CONSENT

The patient has agreed and signed a written informed consent regarding this study publication.

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AUTHOR CONTRIBUTION

All authors contributed equally in this manuscript writing and publication process.

CONFLICT OF INTEREST

None to declare.

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