Complicated Pregnancy in a Patient with Distal Renal Tubular Acidosis, Systemic Lupus Erythematosus, and Antiphospholipid Syndrome: A Rare Case and Management Strategies

I Gede Yasa Asmara,[1,2*] Alvina Widhani,[3] Lugyanti Sukrisman,[4] Maruhum Bonar H. Marbun[5]

[1]Department of Internal Medicine, Faculty of Medicine, University of Mataram - West Nusa Tenggara General Hospital, Mataram, Indonesia.
[2]Fellow of Nephrology and Hypertension, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia – Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia.
[3]Division of Allergy and Clinical Immunology, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia – Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia.
[4]Division of Hematology and Medical Oncology, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia – Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia.
[5]Division of Nephrology and Hypertension, Department of Internal Medicine, Faculty of Medicine, Universitas Indonesia – Dr. Cipto Mangunkusumo Hospital, Jakarta, Indonesia.

Corresponding Author:
I Gede Yasa Asmara, MD, MMed, FINASIM. Department of Internal Medicine, Faculty of Medicine, University of Mataram - West Nusa Tenggara General Hospital, Mataram, Indonesia. Jl. Pendidikan No. 37 Mataram, West Nusa Tenggara 83125, Indonesia. E-mail: yasa.asmara@unram.ac.id

ABSTRACT

Distal renal tubular acidosis (dRTA) is a rare disorder characterized by impaired acid excretion leading to metabolic acidosis and hypokalemia. Its occurrence during pregnancy, particularly alongside systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS), poses significant challenges for both maternal and fetal outcomes. This case report describes the successful management of a 23-year-old woman with secondary dRTA, SLE, and APS during pregnancy. The patient, with a history of recurrent hypokalemia and previous preterm deliveries, was closely monitored by a multidisciplinary team. Throughout her pregnancy, she required significant potassium and bicarbonate supplementation to maintain electrolyte and acid-base balance. Additionally, hydroxychloroquine, methylprednisolone, aspirin, and unfractionated heparin were continued to manage SLE and APS. Despite the complexity of her condition, she delivered a healthy baby girl at 37 weeks via cesarean section. This case provides valuable insights into managing dRTA during pregnancy, highlighting the importance of customized approaches to the management of electrolyte and acid-base abnormalities, as well as that of autoimmune disease.

Keywords*: Antiphospholipid Syndrome, Acidosis, Renal Tubular, Hypokalemia, Pregnancy, SLE.*

INTRODUCTION

Distal renal tubular acidosis (dRTA) is a rare renal disorder characterized by an inability of the distal tubules to excrete hydrogen ions, resulting in metabolic acidosis and hyperchloremia.[1] Its occurrence during pregnancy is particularly uncommon, and when combined with systemic lupus erythematosus (SLE) and antiphospholipid syndrome (APS), it presents a unique clinical challenge.[2,3] Pregnancy

induces significant physiological changes in renal function, including disruptions in acid-base homeostasis and electrolyte balance, which can exacerbate dRTA symptoms.[4] Untreated maternal acidosis during pregnancy can result in adverse outcomes, such as impaired fetal growth, reduced bone mineralization, and preterm delivery.[5,6] Despite these risks, successful pregnancies in women with dRTA are rarely documented. This case report details the clinical course and multidisciplinary management of a 23-year-old woman with secondary dRTA related to SLE and APS, who successfully delivered a healthy infant. This case highlights the importance of timely diagnosis, continuous monitoring, and a collaborative multidisciplinary approach.

CASE ILLUSTRATION

A 23-year-old woman presented with progressive weakness in both legs over five months. She reported difficulty walking and intermittent fatigue that worsened during her pregnancy. Her medical history revealed hypokalemia diagnosed eight years earlier. Since then, she had been regularly taking bicarbonate and potassium supplements until late 2019, during which her serum potassium levels stabilized between 3.2 and 3.4 mmol/L. From January 2020 to July 2022, the patient discontinued regular potassium supplementation, as random evaluations showed the potassium level was within normal limits (3.6–4.1 mmol/L). Her obstetric history included two previous pregnancies. In 2020, her first pregnancy resulted in a preterm delivery at 36 weeks via cesarean section due to fetal distress. The newborn, diagnosed with congenital heart disease (CHD), succumbed after one day of NICU treatment. In 2021, her second pregnancy ended with preterm delivery at 34 weeks, with the newborn passing away from sepsis and CHD after four days of NICU treatment. The patient reported intermittent joint pain and skin bruising during her second pregnancy, raising suspicion of an autoimmune condition. In February 2022, she was started on hydroxychloroquine (HCQ; 200 mg daily), colchicine (0.5 mg/day), calcitriol (0.25 mcg/day), calcium carbonate (500 mg/day), sulfasalazine (250 mg twice/day), methylprednisolone (4 mg daily), and risedronate sodium (35 mg/week). She was subsequently diagnosed with APS and was prescribed acetylsalicylic acid (80 mg/day). The patient did not have the opportunity for formal pregnancy planning, as it was discovered that her menstrual cycle was late, indicating a pregnancy of approximately 14 weeks as of August 2022. At the initial assessment, her clinical immunologist discontinued colchicine, sulfasalazine, and Actonel. Subsequent consultations with the Obstetrics and Gynecology department were initiated, and the patient received supplements, namely a supplement consisting of 75 mg docosahexaenoic acid, 7 mg eicosapentaenoic acid and 100 mg arachidonic acid p.o.o.d., vitamin D3 supplement 5000 IU p.o.o.d., units), zinc 20 mg p.o.o.d, as well as a multivitamin tablet containing 1 mg folic acid p.o.o.d. Following this, she engaged in routine antenatal care every 1-2 weeks, tailored according to her gestational age, where obstetricians conducted regular ultrasounds and laboratory tests to monitor maternal health, fetal growth, and potential risks of preeclampsia. Throughout the pregnancy, she experienced recurrent episodes of leg weakness, which improved temporarily with potassium supplementation. She was referred to the nephrology clinic for further evaluation of the persistent hypokalemia.

Physical examination revealed normal vital signs and mild bilateral pitting edema. Neurological findings were unremarkable except for subjective leg weakness. There were no signs of active joint inflammation or lupus-related skin manifestations such as malar rash or alopecia. Laboratory results revealed a hemoglobin level of 13.2 mg/dL, leukocyte count of 14,700 cells/μL, and platelet count of 346,000 cells/μL. Urinalysis revealed a yellow, clear appearance with a specific gravity of 1.005, a pH of 7.5, negative albuminuria, leukocyte sediment of 6–7 cells/HPF, and erythrocytes of 0–1 cells/HPF. Blood gas analysis results were consistent with metabolic acidosis, revealing a pH of 7.33, pCO2 of 22.1 mmHg, pO2 of 104.5, and an HCO3 level of 12 mmol/L. Serum electrolytes showed hypokalemia, with a potassium level of 2.7 mmol/L, while sodium and chloride levels were 135 mmol/L and

113 mmol/L, respectively. Renal function tests revealed mild impairment, with a urea level of 47.1 mg/dL, serum creatinine of 1.3 mg/dL, and an estimated glomerular filtration rate (eGFR) of 58 mL/min/1.73 m². The thyroid profile was within normal limits, with a thyroid-stimulating hormone (TSH) level of 2.02 mg/dL and a free thyroxine (FT4) of 0.96 mg/dL. Autoimmune screening yielded negative rheumatoid factor (RF), but positive anti-Smith (Sm) antibody and weakly positive lupus anticoagulant (LA) in two separate assays. Radiography of the bone revealed diffuse osteopenia. Renal ultrasonography showed bilateral nephrocalcinosis.

The patient was diagnosed with dRTA, secondary to SLE and APS. At diagnosis, the patient was at 26 weeks of gestation. She was started on oral potassium supplements (1200 mg, three times daily) and sodium bicarbonate (1000 mg, three times daily) to correct persistent hypokalemia and metabolic acidosis. Given the mild nature of her SLE, limited to musculoskeletal involvement, with SLEDAI-2K score of zero, HCQ was continued at 200 mg/day, and methylprednisolone was tapered gradually to a maintenance dose of 4 mg twice a week. Due to her APS history and increased risk of thrombosis during pregnancy, the patient was prescribed low-dose aspirin (80 mg/day) and subcutaneous heparin (5000 units twice daily) as a prophylaxis against thrombotic complications. Folic acid, vitamin D, and calcium supplements were prescribed to mitigate the risk of bone demineralization associated with chronic acidosis. The patient was closely monitored by a multidisciplinary team comprising nephrologists, immunologists, hematologists, obstetricians, and pediatricians. Regular assessments of electrolytes and kidney function were performed to ensure that serum potassium and bicarbonate levels remained within normal limits (**Table 1**).

At 37 weeks of gestation, the patient underwent an elective cesarean section, delivering a healthy baby girl weighing 2,850 g with an Apgar score of 8/9. Postoperatively, the patient was closely monitored for electrolyte imbalance, and her potassium and bicarbonate supplements were adjusted accordingly. Her kidney function remained stable, with a creatinine level of 1.3 mg/dL and eGFR of 58 mL/min/1.73 m². During the postpartum period, potassium and bicarbonate supplementation were gradually decreased as serum potassium levels stabilized. Her SLE was well-controlled with HCQ and a low dose of methylprednisolone, maintaining a SLEDAI-2K score of zero during several follow-ups. At her one and a half year postpartum, serum potassium was 3.0 mmol/L, bicarbonate level was 19.4 mmol/L, and ultrasonography revealed stable

Table 1. Laboratory monitoring during pregnancy

Gestational age	Bicarbonate (mmol/L)	Potassium (mmol/L)	Urine pH	Creatinine (mg/dL)	eGFR (ml/min)
16 week	14.1	3.3	7.0	1.3	58.0
20 week	-	2.9	7.5	-	-
22 week	-	2.7	-	1.3	58.0
26 week	-	3.7	8.0	-	-
27 week	20.6	3.8	7.5	-	-
31 week	11.7	3.4	7.0	1.6	44.8
35 week	12.0	3.6	7.0	1.5	48.4
37 week	-	3.3	7.5	1.4	52.6

Table 2. Laboratory monitoring post-partum

Post-partum	Bicarbonate (mmol/L)	Potassium (mmol/L)	Urine pH	Creatinine (mg/dL)	eGFR (ml/min)
2 week	19.8	3.2	-	-	-
3 week	-	-	-	1.3	57.6
4 week	-	3.0	7.0	1.2	63.4
6 week	-	3.2	-	1.3	57.6
1 year	-	2.8	7.5	1.3	57.2
1.5 year	19.4	3.0	7.0	1.3	58.5

nephrocalcinosis without progression. Regular multidisciplinary care continued, focusing on renal function and electrolyte monitoring (**Table 2**).

Following birth, the infant developed a fever and experienced a urinary tract infection, which subsequently progressed to bacterial sepsis. Fortunately, the patient's condition stabilized by pediatricians following the administration of appropriate antibiotics and supportive therapies, leading to discharge after a three-week hospitalization. Diagnostic evaluations, including echocardiography conducted on 23 February 2023 and 10 March 2023, indicated no abnormalities. Concurrent screenings for potential anomalies in the realms of otolaryngology, as well as cranial and renal ultrasounds, also yielded normal results.

DISCUSSION

Distal renal tubular acidosis is a rare disorder characterized by the inability of the kidneys to excrete hydrogen ions effectively, resulting in hyperchloremic metabolic acidosis. This defect leads to compensatory loss of bicarbonate and potassium, causing chronic hypokalemia.[1] Distal RTA is rarely encountered during pregnancy, more commonly linked to substance abuse, such as toluene, and less frequently associated with SLE.[7] Distal RTA due to maternal substance abuse has been associated with fetal growth retardation, preterm labor, dysmorphic features, and perinatal death. This may be related to the direct toxic effect on fetal tissues, RTA, or due primarily to underlying renal disease.[8] Antiphospholipid Syndrome did not pose a contraindication for pregnancy in this patient. It is recommended that individuals with positive antiphospholipid antibodies receive low-dose aspirin during pregnancy to mitigate risks. This patient had been consistently taking low-dose aspirin prior to confirming her pregnancy, and this regimen was sustained throughout her gestation. Furthermore, given her stable SLE with low disease activity, she was deemed fit to undertake pregnancy.[20] Distal RTA during pregnancy presents a unique clinical challenge, especially when associated with autoimmune diseases like SLE and APS. The combination of these conditions, as seen in this case, highlights the complexity of managing a pregnancy with coexisting diseases, particularly in maintaining electrolyte balance and avoiding maternal and fetal complications.

Pregnancy Implications and Effect on Maternal and Fetal Outcomes

During pregnancy, physiological changes in renal function, such as increased GFR and enhanced bicarbonate excretion, further exacerbate dRTA.[9] Normally, pregnancy induces a 40–50% increase in GFR by the ninth week of gestation, accelerating bicarbonate excretion and reducing serum bicarbonate concentration from a baseline of approximately 30 mmol/L to 20 mmol/L.[10] Additionally, pregnant women experience respiratory alkalosis due to increased minute ventilation, further complicating the acid-base balance. Decreased bicarbonate levels during pregnancy can exacerbate metabolic acidosis in patients with dRTA.[11]

Untreated maternal metabolic acidosis during pregnancy adversely affects fetal outcomes. Acidosis can impair uterine blood flow and reduce oxygen and nutrient supply to the fetus, which may result in intrauterine growth restriction (IUGR) and fetal distress.[12,13] In addition, chronic maternal acidosis has been associated with impaired fetal bone development owing to decreased calcium reabsorption and increased calcium release from maternal bones to buffer excess hydrogen ions. This condition can lead to osteomalacia in the mother and rickets in the fetus.[3,14] In the present case, the patient's metabolic acidosis and hypokalemia were effectively managed with potassium and bicarbonate supplementation to prevent severe fetal complications. However, given the patient's history of two previous preterm deliveries and neonatal deaths due to CHD and sepsis, the risk of preterm delivery and fetal morbidity remained significant.

Impact of SLE and APS on Pregnancy

SLE and APS add complexity to the pregnancy management. SLE exacerbates the inflammatory response during pregnancy, increasing the risk of pregnancy-related complications such as preeclampsia, IUGR, and preterm birth.[15] APS, an autoimmune disorder characterized by recurrent thrombosis and pregnancy morbidity, also played

a significant role in this patient's clinical course. The presence of antiphospholipid antibodies increases the risk of placental insufficiency, preeclampsia, and recurrent miscarriages.[16] In this case, dRTA was likely secondary to SLE. The pathophysiology involves immune-mediated damage to the hydrogen ATPase pump in type A intercalated cells and the presence of autoantibodies against the carbonic anhydrase II enzyme.[17] The APS in this case was also secondary to SLE. The recurrent hypokalemia noted eight years ago could have been an undiagnosed dRTA and the initial indicator of SLE.[18] In this case, the patient's history of two previous neonatal losses, combined with the diagnosis of APS, placed her at high risk for further pregnancy complications. Distal RTA, SLE, and APS independently increase the risk of preterm labor and pregnancy complications. The interaction between these conditions further highlights the necessity of vigilant monitoring and a multidisciplinary approach to care.

Management and Prognosis

The management of dRTA during pregnancy focuses on correcting the acid-base and electrolyte imbalances, particularly hypokalemia and metabolic acidosis.[19] In this case, the patient required significant potassium and bicarbonate supplementation throughout her pregnancy. Potassium and bicarbonate requirements may increase sevenfold and 4.5-fold, respectively.[11] In terms of pharmacological management, methylprednisolone and HCQ were continued throughout the pregnancy to control SLE activity. Literature suggests that less than 10% of the prednisolone dosage is transmitted to fetal circulation.[20] While there is a slight elevation in the risk of miscarriage associated with steroid use, this does not correlate with an increased incidence of congenital malformations, particularly at the low weekly dose of 8 mg used for this patient. Higher doses of prednisone (> 10 mg/day) have been associated with gestational hypertension, gestational diabetes, premature rupture of membranes, and smaller-than-gestational-age (SGA) newborns.[15] Hydroxychloroquine has not been shown to increase the risks of miscarriage or congenital abnormalities and has demonstrated efficacy in reducing the incidence of congenital heart block in fetuses.[20] Tissue damage related to SLE and preeclampsia is thought to be mediated by reactive oxygen species (ROS), and several studies indicate that HCQ may mitigate this damage by reducing the synthesis of ROS.[15] Low-dose aspirin and heparin were essential in reducing the risk of thrombotic complications associated with APS.[16] Renal ultrasound follow-up during pregnancy revealed nephrocalcinosis, a common complication of dRTA caused by excessive calcium excretion and deposition in the renal parenchyma.[21]

The prognosis of patients with dRTA during pregnancy can be favorable if metabolic acidosis and electrolyte imbalances are adequately corrected.[3,19] There are no definitive guidelines outlining the criteria for pregnancy termination in cases involving dRTA and APS. However, termination may be warranted in SLE patients facing severe pulmonary hypertension, significant restrictive lung disease, severe renal insufficiency (eGFR < 30 mL/min/1.73 m^2), advanced heart failure, previous pulmonary embolism, or hemolysis, elevated liver enzymes, low platelet count (HELLP) syndrome despite appropriate treatment, as well as confirmed congenital heart block via fetal echocardiography between 18-26 weeks' gestation.[15]

As demonstrated in this case, timely diagnosis and appropriate management enabled the patient to successfully carry her pregnancy to term, resulting in the delivery of a healthy baby via cesarean section. Regular follow-up and monitoring of kidney function, electrolyte levels, and SLE activity are essential to prevent further complications.[2] The patient will require lifelong potassium and bicarbonate supplementation to maintain normal electrolyte balance.[12] In addition, ongoing anticoagulation therapy for APS will be necessary to reduce the risk of future thrombotic events, particularly during subsequent pregnancies.[15] The role of pediatricians is also pivotal within a multidisciplinary framework focused on the early detection and management of CHD and other congenital anomalies. Following discharge, the infant underwent routine evaluations by a pediatrician every 2 to 4 weeks. At 1.5 years of age, she showed normal growth patterns and developmental milestones.

CONCLUSION

This case highlights the complex interplay among dRTA, SLE, and APS during pregnancy. Successful management of such high-risk cases highlights the importance of early diagnosis, aggressive correction of metabolic and electrolyte imbalances, and a multidisciplinary care approach. While the prognoses for both the mother and child were positive in this case, long-term follow-up remains critical for managing the potential complications associated with dRTA, SLE, and APS.

CONFLICT OF INTERESTS

The authors have no conflicts of interest to declare.

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