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Managing unbiopsied nephrotic syndrome in High-Risk twin pregnancy: A case report

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Abstract

Nephrotic Syndrome (NS) complicating twin pregnancy presents significant multidisciplinary challenges. We report a 24-year-old G2P1 patient with pre-existing NS (unbiopsied, diagnosed 2021) admitted at 17-18 weeks' gestation with exacerbated edema, massive proteinuria (6g/24h), critical hypoalbuminemia (0.93 g/dL), and bilateral pleural effusion. Key interventions included IV methylprednisolone (62.5 mg/day tapered to oral), albumin 20% transfusions, strict fluid restriction (≤600 mL/day), high-protein diet (1900 kcal + 5g/day supplement), and alternate-day aspirin 80 mg for preeclampsia prophylaxis under nephrology- obstetrics co-management. By day 17, albumin improved to 2.79 g/dL with proteinuria reduction to 0.3g/24h, enabling discharge on oral therapy while maintaining twin pregnancy toward 34-week delivery targets.

Keywords: Nephrotic syndrome, Twin pregnancy, Multidisciplinary care, Methylprednisolone

Introduction

Nephrotic syndrome is characterized by edema, heavy proteinuria, hypoalbuminemia, and often hyperlipidemia. The diagnosis is established based on the characteristic clinical picture confirmed by heavy proteinuria and hypoalbuminemia (Kodner, 2016).

The occurrence of nephrotic syndrome due to primary kidney disease in pregnancy is very rare (0.028%). Differentiation from preeclampsia is challenging without histological examination; however, the onset of proteinuria before 20 weeks of gestation suggests primary glomerular disease. Although protein excretion frequently increases during pregnancy in this condition, and elevated creatinine is a risk factor for poor prognosis, renal function is generally better-preserved in pregnant patients (Siligato et al., 2020; Mohapatra and Samantaray, 2020).

Nephrotic syndrome in pregnancy increases the risk of maternal complications (worsening renal function) and fetal complications (prematurity, low birth weight, fetal growth restriction). Management requires a multidisciplinary approach (nephrology and obstetrics) to mitigate risks and necessitates early planning (De Castro et al., 2017; Rovin et al., 2021; Kahil, 2025).

Case report

A 24-year-old woman, pregnant with twins (second pregnancy), complains of edema starting 2 years ago that worsened 2 days prior to hospital admission. Referred from Tongas District Hospital, Probolinggo, with diagnoses of nephrotic syndrome + hypoalbuminemia + gravid. Edema begins in the eyelids in the morning and shifts to the lower limbs after walking. History of nephrotic syndrome diagnosed in 2021 without renal biopsy. The patient denies of diabetic, hipertention, dyspnea, abdominal rigidity, ruptured membranes, hair loss, joint pain, facial erythema, fever, jaundice, right upper quadrant (RUQ) pain, and tea-colored urine. The patient is a housewife with two marriages. Her first marriage ended due to widowhood, and she has one 3-year-old child from that union. She is currently in her second pregnancy (with twins) by her current husband. She has attended seven Antenatal Care (ANC) visits and was diagnosed with a high-risk pregnancy by an obstetrics-gynecology specialist due to Twin gestation and underlying nephrotic syndrome.

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Upon arrival at the Emergency Department of Dr. Soetomo General Hospital, the patient was in fair general condition with GCS E4V5M6, blood pressure 123/80 mmHg, pulse 88/minute, respiratory rate 20/minute, temperature 36.5°C, and oxygen saturation 98-99% on room air. Weight was 44 kg with height 140 cm (BMI 22.4 kg/m^2). Physical examination revealed slightly anemic conjunctivae without scleral icterus, cyanosis, or cervical lymphadenopathy. Heart sounds included singular S1 and S2 without murmurs, gallops, or extrasystoles. Vesicular breath sounds were present bilaterally without rales or wheezing. The abdomen was convex with normal bowel sounds; liver and spleen were non-palpable. Extremities showed warm acral areas with mild pallor, capillary refill time <2 seconds, and bilateral pitting edema.

Laboratory results indicated anemia (Hb 9.1 g/dL), leukocytosis (13,920/mm^3) with neutrophilia (90.3%), thrombocytosis (517,000/mm^3), hyponatremia (Na 131 mmol/L), and severe hypoalbuminemia (0.93 g/dL). Urinalysis demonstrated 4+ proteinuria and 2+ hematuria with ACR ≥300 and PCR ≥0.5. Arterial blood gas analysis showed respiratory alkalosis (pH 7.49; pCO_2 34) with hypoxemia (pO_2 80 mmHg; P/F ratio 380). ECG revealed sinus tachycardia (125/minute) with normal axis, while chest X-ray disclosed early pulmonary edema and bilateral pleural effusion without cardiac abnormalities.

The obstetric-gynecologic consultation revealed no vaginal bleeding or discharge. Fetal heart rates were 134 bpm for the first twin and 139 bpm for the second twin, with no uterine contractions (Braxton Hicks). Transvaginal ultrasound demonstrated that Twin I estimated gestational age 18-19 weeks (BPD 4.06 cm, HC 15.58 cm, AC 12.27 cm, FL 2.66 cm), estimated weight 201 g, and amniotic fluid index (SDP) 5.25 cm. Twin II: Estimated gestational age 17-18 weeks (BPD 3.92 cm, HC 13.64 cm, AC 12.54 cm, FL 2.56 cm), estimated weight 201 g, and SDP 5.25 cm. The placenta was positioned from the fundus to posterior corpus, with monochorionic diamniotic (MCDA) pregnancy confirmed by the T-sign.

The patient was diagnosed with nephrotic syndrome (Alb 0.93 g/dL), normocytic anemia (Hb 9.2 g/dL), thrombocytosis (517k/µL), bilateral pleural effusion, and diamniotic twin pregnancy at 17-18 weeks (G2P1). Management included Oxygen supplementation, High- protein diet (1900 kcal/day), IV 20% albumin (100 mL/4 hours), Methylprednisolone 62.5 mg IV daily, and Oral hematinics (ferrous fumarate 400 mg, calcium 1000 mg, folate 400 mcg daily) under joint care with OB-GYN.

On hospital day 2, the patient remained conscious with persistent edema and stable weight (44 kg). Laboratory findings revealed worsening anemia (Hb 8.2 g/dL), hypokalemia (K^+ 3.10 mmol/L), and persistent dyslipidemia (LDL 258 mg/dL, triglycerides 370 mg/dL). Notable improvements included rising albumin (1.15 g/dL vs. 0.93 baseline) and normalized sodium (140 mmol/L). Immunology workup showed borderline low C3 (80 mg/dL) with normal ANA. The patient continues previous therapies with the addition of oral potassium replacement at 600 mg three times daily.

On Day 3, the patient reported stable edema and no dyspnea, with neutral fluid balance and improved albumin (1.41 g/dL post-transfusion). Fetomaternal ultrasound showed no major fetal anomalies, though cardiac reassessment (LVOT/RVOT) was scheduled for 24 weeks. By Day 4, lower limb edema worsened (+100 mL fluid balance) with critical anemia (Hb 6.9 g/dL) and severe proteinuria (6g/24h). Lab results showed persistent hypoalbuminemia (1.64 g/dL), hypokalemia (K^+ 3.30 mmol/L), and leukocytosis (14,020/mm^3). Interventions were escalated to Strict fluid restriction (≤600 mL/day) and high-protein diet (1900 kcal + 5g protein supplement), Daily PRC transfusions (target Hb ≥10g/dL), IV furosemide 20 mg BID, and Expanded diagnostics: Coombs test, cultures, FOBT, and hepatic/renal panels. All prior therapies (steroids, albumin transfusions if Alb <2.5 g/dL, hematinics) continue under OB- GYN co-management for the 17-18-week twin pregnancy.

On hospital day 5, the patient reported no worsening edema or dyspnea, with significant negative fluid balance (-1200 mL/24h). Laboratory results showed improved anemia (Hb 9.4 g/dL), persistent leukocytosis (13,970/mm^3) with neutrophilia (77.3%), thrombocytosis (573,000/mm^3), and ongoing hypoalbuminemia (1.61 g/dL). Peripheral blood smear revealed normochromic normocytic anemia with polychromasia, leukocytosis with immature granulocytes

(myelocytes/metamyelocytes), and reactive thrombocytosis without blasts or giant platelets. Renal/liver function remained normal (creatinine 0.2 mg/dL, BUN 7 mg/dL), and fecal occult blood was negative. All prior therapies continue.

On day 9, the patient exhibited productive cough with mild dyspnea but stable edema and weight loss (40 kg), alongside negative fluid balance (-900 mL/24h). Labs revealed improved Hb (11.1 g/dL), severe hypoalbuminemia (1.58 g/dL), critical hypertriglyceridemia (821 mg/dL), and persistent nephrotic-range proteinuria (5.2g/24h). Multidisciplinary consensus transitioned IV furosemide to oral 40 mg daily, initiated alternate-day aspirin 80 mg (balancing thrombosis/bleeding risks), added ceftriaxone 2g IV BID and NAC 600 mg PO daily, and coordinated pravastatin with OB-GYN. Pregnancy management targets 34 weeks with biweekly monitoring, preparing for outpatient transition with local hospital coordination while continuing prior therapies and steroid oral conversion.

On hospital day 11, the patient reported reduced cough, no fever, and decreased edema, with weight stabilizing at 38 kg but a concerning positive fluid balance (+400 mL/24h). Laboratory results showed persistent dyslipidemia (triglycerides 569 mg/dL, total cholesterol 274 mg/dL) and ongoing hypoalbuminemia (1.92 g/dL), though albumin levels were improving. Electrolytes revealed mild hyponatremia (Na^+ 137 mmol/L) and hypokalemia (K^+ 3.30 mmol/L), while renal function remained normal (creatinine 0.6 mg/dL, BUN 7.0 mg/dL) and urine culture was negative. Therapy adjustments included reducing oral furosemide to 20 mg daily and initiating pravastatin 20 mg daily per OB-GYN coordination, though the latter was unavailable at the hospital.

By Day 13, the patient reported reduced cough and edema without dyspnea or fever, though fluid balance turned positive (+100 mL/24h). Labs showed improving albumin (2.34 g/dL) but persistent anemia (Hb 9.6 g/dL), hypokalemia (K^+ 3.10 mmol/L), and hyponatremia (Na^+ 137 mmol/L). A proposed gemfibrozil regimen was declined after OB-GYN consultation.

On Day 16, all symptoms resolved with significant albumin rise (2.79 g/dL) and dramatic proteinuria reduction (0.3g/24h), prompting methylprednisolone taper to 48 mg/day orally.

By Day 17, the patient achieved clinical stability and was cleared for discharge on oral therapy: methylprednisolone 48 mg/day, furosemide 20 mg/day, supplements (ferrous fumarate 400 mg, calcium 1000 mg, folate 400 mg, potassium 1800 mg daily), and alternate-day aspirin 80 mg.

Discussion

Nephrotic Syndrome (NS) is rare in pregnancy (incidence 0.028%), posing diagnostic dilemmas due to overlapping features with preeclampsia. Differentiation between primary glomerular disease and preeclampsia requires renal biopsy, despite potential fetal risks. Significant proteinuria before 20 weeks' gestation strongly indicates primary glomerular disease. Renal biopsy remains a valuable diagnostic tool with strict patient selection due to maternal-fetal complication risks (Siligato et al., 2020; De Castro et al., 2017).

Nephrotic syndrome	Nephrotic-range proteinuria	Non-nephrotic-range proteinuria
Proteinuria (adults)* • ≥3.5 g per 24 h • PCR ≥3000 mg/g (≥300 mg/mmol)	Proteinuria (adults) • ≥3.5 g per 24 h • PCR ≥3000 mg/g (≥300 mg/mmol)	Variable levels of proteinuria • 0.3–3.4 g per 24 h • PCR <300 mg/g (<30 mg/mmol)
Proteinuria (children)* • ≥40 mg/m²/h • ≥300 mg/dl • 3+ on urine dipstick • PCR ≥2000 mg/g (≥200 mg/mmol)	Proteinuria (children) • ≥40 mg/m²/h • ≥300 mg/dl • 3+ on urine dipstick • PCR ≥2000 mg/g (≥200 mg/mmol)	• Serum albumin normal • No clinical symptoms
• Hypoalbuminemia† • Edema‡ • Hyperlipidemia‡	• Serum albumin usually normal • Edema is usually absent or minor • Serum lipids usually normal or only mildly elevated	

Figure 1. Characteristic of nephrotic syndrome, nephrotic-range proteinuria, and non-nephrotic-range proteinuria (Rovin et al., 2021)

The patient exhibited classic NS manifestations massive proteinuria (6g/24h), critical hypoalbuminemia (0.93 g/dL), generalized edema, and bilateral pleural effusion. Pre- pregnancy NS history without biopsy complicated management. Initial therapy focused on High-protein diet (1900 kcal + 5g/day supplement) to counter malnutrition, ACEi/ARB avoidance due to fetal teratogenic risks, Edema control via fluid restriction (600 mL/day) and

loop diuretics (Attini et al., 2017; Kaul et al., 2021; Jam et al., 2025).

NS-related edema stems from dual mechanisms: hypoalbuminemia and sodium retention. This patient received FDA Category C 20% albumin transfusions under rigorous risk-benefit assessment, elevating albumin to 2.79 g/dL. IV furosemide targeted sodium retention through Na-K-Cl cotransporter inhibition in Henle's loop, achieving negative diuresis (-1200 mL/24h) without compromising fetal perfusion (Gupta et al., 2019; Perinandika et al., 2017).

High-dose IV methylprednisolone (62.5 mg/day) induced positive clinical response, transitioned to oral dosing. Steroid safety in pregnancy is supported by placental metabolism via 11β-HSD2 enzyme. Alternate-day aspirin (80 mg/48h) was implemented for preeclampsia prevention (35% risk reduction), with dose modification mitigating GI bleeding risk from steroid interaction (Ponticelli & Moroni, 2018; Rovin et al., 2021).

Refractory hyperlipidemia (triglycerides 821 mg/dL) warranted statin therapy. Pravastatin 20 mg/day was selected for dual action as Dyslipidemia correction, and Angiogenic factor modulation (↑PlGF/↓sFlt-1) for preeclampsia prevention. Despite FDA removal of pregnancy contraindications for statins, implementation was hindered by local unavailability (Mészáros et al., 2023; Busuioc et al., 2023).

Successful management required tight nephrology-obstetrics coordination with goals: (1) Maintain pregnancy until 34 weeks; (2) Biweekly renal monitoring; (3) Structured inpatient-outpatient transition. Patients without hypertension/severe renal impairment show favorable maternal-fetal outcomes, emphasizing preconception counseling and disease control pre-pregnancy (Sato et al., 2017; Rovin et al., 2021).

Per current evidence and case experience, we recommend: (1) Selective renal biopsy for early-pregnancy NS; (2) Albumin transfusion only for symptomatic hypoalbuminemia; (3) Rigorous preeclampsia screening with low-dose aspirin; (4) Pravastatin consideration for refractory hyperlipidemia; (5) Collaborative care models as the gold standard.

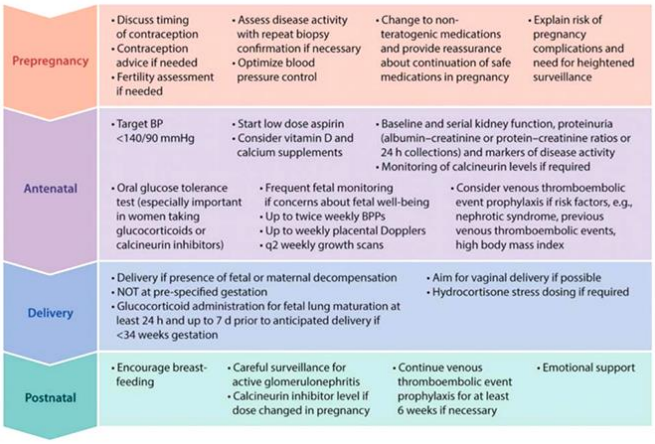

Figure 2. Coordinated care for pregnant patients with glomerular disease (Rovin et al., 2021)

Conclusion

This case demonstrates that aggressive multidisciplinary management—early high-dose corticosteroids, targeted albumin replacement, and preeclampsia prophylaxis—can achieve clinical remission of nephrotic syndrome in high-risk twin pregnancy despite diagnostic limitations (unavailability of renal biopsy and statins). Critical lessons include: 1) Steroid responsiveness supports empirical treatment when biopsy is deferred, 2) Aspirin dosing modifications balance thrombosis/bleeding risks with immunosuppression, and 3) Preconception optimization remains essential for glomerulopathy patients considering pregnancy, with collaborative care models being paramount for maternal-fetal success.

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