

Intrahepatic cholestasis of pregnancy in a chronic kidney disease patient: A case report

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Abstract The pregnancy-specific liver condition known as intrahepatic cholestasis of pregnancy (ICP) is characterized by pruritus throughout the third trimester of pregnancy and elevated serum transaminases. ICP in patients with CKD can obscure the diagnosis. Fetal risks whose mothers suffer from ICP must be monitored. **Case:** 32-year-old woman 29 weeks pregnant with a history of CKD and routine hemodialysis, complaints of itching appeared on the palms and legs that extended into the abdomen and back in the final trimester of pregnancy. The serum transaminase results are within normal limits. Topical emollients are given as therapy. Babies are born prematurely with low birth weight and asphyxia. The baby dies at the age of 3 days. The patient's itching complaints are reduced after delivery. **Discussion:** The diagnosis of ICP is based on pruritus complaints on both palms and feet in late trimester pregnancy. Increased serum aminotransferase levels are a clue to the diagnosis. Normal serum aminotransferase is due to a deficiency in its coenzyme formation due to CKD. ICP therapy is non-specific and systemic. Increased levels of maternal bile acids cause the failure of pulmonary surfactant and increase oxytocin resulting in premature labor. Chorionic venous vasoconstriction and placental oxidative stress cause low birth weight in infants. **Conclusion:** Pruritus with or without skin changes in the last trimester of pregnancy should consider the possibility of ICP. CKD patients have normal or lower serum aminotransferase levels. Strict supervision of the fetus should be carried out.

Key words

ICP, CKD, pruritus, obstetric cholestasis, pruritus uremicum.

Introduction

The term "intrahepatic cholestasis of pregnancy" (ICP), commonly referred to as "obstetric cholestasis, prurigo gravidarum," refers to generalized pruritus without active or hepatotoxic hepatitis and with or without jaundice. Abnormal biochemistry is present, followed by spontaneous resolution after delivery, and may recur in subsequent pregnancies.^{1,2} This disorder usually occurs in the second or third trimester of pregnancy.³ This

rare condition may increase the risk of meconium-staining, premature birth, emergency fetus, and fetal death.⁴ The incidence of ICP varies worldwide between 0.2% and 25%, with the most significant prevalence of up to 25% in the Araucania race in South America. Its majority in Europe is 0.5% to 1.5% of all pregnancies, and the highest incidence has been reported in Sweden. The incidence of ICP in China is considered typical, with an incidence of 2.3% to 6.0%.¹

Pregnancy in chronic kidney disease (CKD) is rare. The incidence of pregnancy-associated ICP in CKD has been reported in 18% of 67 pregnancies.⁵ The pathogenesis between the two is unclear. Pruritus, the main complaint, is also found in CKD patients. Physiological changes in

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CKD cause the diagnosis of ICP to be inconsistent with existing criteria.

Case Report

A 32-year-old woman presented with itching all over the body. She was 29 weeks pregnant and had CKD two years ago. The patient underwent hemodialysis three times a week during this pregnancy. Entering the third trimester of pregnancy, the patient begins to feel itching which is dominant on the palms and feet and then spreads to the back, abdomen, and extremities. Itching is felt all the time and feels worse at night, interfering with sleep. The patient took cetirizine to reduce itching, but there was no improvement. Pale stools, dark urine such as tea, body and eye mucosa becomes yellow is denied. The patient has anuria. The patient was treated at a different Yogyakarta hospital three months before the complaint due to complaints of upper right abdominal pain.

The ultrasound examination (USG) showed swelling of the bile and the fetus at 20 weeks gestation. It is also known that the baby's heart valve has problems, and the fetal weight does not match the gestational age. The patient was diagnosed with CKD two years ago due to preeclampsia and routinely underwent hemodialysis twice a week. The patient denied complaints of itching before and after hemodialysis. Hemodialysis began three times a week, and she received monthly blood transfusions. The patient received an Epoetin injection twice a week and heparin every hemodialysis. The patient's general condition is good, conscious with vital signs within normal limits. Dermatological examination showed a skin xerosis impression. The abdominal region showed linear excoriation and striae gravidarum. The left forearm flexor shows an arteriovenous shunt (AV-shunt). The left wrist flexor showed an aneurysm (**Figure 1**). The visual analog scale (VAS) for pruritus in this patient was 6.

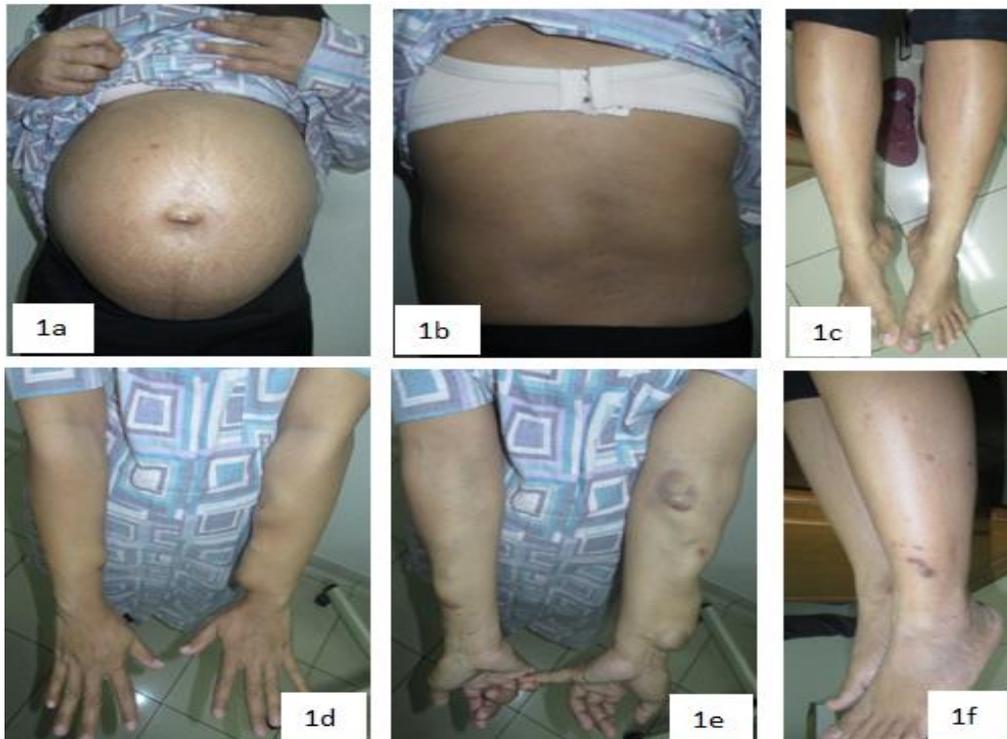


Figure 1. 1a. Excoriated lesions and stria gravidarum. 1b,c&f. Excoriated lesions and hyperpigmented nodules. 1d&e Left forearm flexor shows arteriovenous shunt (AV-shunt). The left wrist flexor shows an aneurysm.

Laboratory examination results found anemia (hemoglobin 9.8 g/dL), direct bilirubin slightly increased 0.75 mg/dL (0.00-0.20 mg/dL), hypoalbumin (albumin 2.62 g/dL) SGOT 21 U/L (15- 37 U/L), SGPT 16 U/L (12-78 U/L), urea 10.3 mg/dL (6-20 mg/dL), creatinine 4.95 mg/dL (0.6-1 mg /dL), HBs Ag non reactive, Anti HIV non reactive, coagulation function within normal limits.

The patient was diagnosed as ICP based on history, physical examination, and laboratory. Topical therapy is given in urea 10% cream, which is applied twice daily. The patient is managed together with an internist and obstetrician. One week after the dermatology polyclinic examination, the patient had premature labor at 30 weeks of gestation spontaneously vaginally. The baby girl was born with a weight of 1297 grams and a body length of 45 cm. Examination showed respiratory distress with tachypnea and an Apgar score of 1/1/5. The neonate was brought to the neonatal intensive care unit and received continuous positive pressure ventilation (CPAP) for two days. The baby gram results showed hyaline membrane disease (HMD) grade 2. The baby died on the third day due to low birth weight and immature lung development.

Complaints of itching began to decrease after the patient gave birth. VAS score for pruritus 2. The patient continued routine hemodialysis three times weekly and used the previously prescribed topical medication. The patient has not returned to the skin and genital polyclinic because he feels that his complaints have improved.

Discussion

Pregnancy with CKD is rare. Chronic kidney disease patients on routine hemodialysis have irregular menstrual cycles and early menopause.⁶ Dialysis is effective in CKD,

improves sexual function and menstrual cycles, and increases fertility. Pregnancy diagnosis in CKD is challenging because serum levels of β -human chorionic gonadotropin (β -hCG) can be elevated even in the absence of pregnancy.⁷

Pregnancy with CKD can cause maternal and fetal complications.^{7, 8} Estela *et al.* reported that 67 pregnancies with CKD found maternal and fetal complications in chronic hypertension, HELLP syndrome, proteinuria, abortion, premature birth, stillbirth, low birth weight, and 12 cases with preeclampsia and ICP.⁸ The pathogenesis of ICP in CKD is unclear. Separately both are influenced by physiological and hormonal changes during pregnancy.^{7,8}

Pregnant women with pruritus and high serum alanine transaminase (ALT) levels should be evaluated for intrahepatic cholestasis of pregnancy (ICP), the most prevalent pregnancy-specific liver illness. Elevated serum bilirubin level in the absence of other hepatobiliary disease confirms the diagnosis of ICP.^{2,4} This disease is expected in the third trimester of pregnancy with a history of intrahepatic cholestasis during a previous pregnancy, history of cholestasis related to oral contraceptive use, personal or family history of biliary disease, viral hepatitis infection C, multiple pregnancies, or in vitro fertilization pregnancies and selenium deficiency. Age above 35 years is at greater risk of ICP.^{1,2,9,10}

Clinical and laboratory testing are used to make the diagnosis of ICP. Clinical symptoms of ICP are characterized by the onset of severe pruritus that suddenly begins on the palms and soles and quickly becomes generalized. Complaints continue throughout pregnancy and may be worse at night. There were no lesions on the skin initially. The intensity of scratching caused secondary skin lesions ranging from excoriations to severe prurigo nodules. The lesions on the

extensor extremities and other locations such as the buttocks and abdomen. Stools such as putty and dark urine should be sought. Jaundice occurs in approximately 10% of patients due to concomitant extrahepatic cholestasis.^{1,2,5,10,11} The most sensitive indicator for the diagnosis of ICP is an increase in serum bile acid levels and routine liver function tests (including transaminases) up to 30%.^{1,2,9} Pruritus will improve 48 hours postpartum, while biochemical markers will improve after 2-4 weeks.¹²

In this case, the patient realized that she was pregnant at 20 weeks gestation on ultrasound and also found bile swelling. Entering the final trimester, complaints of itching start on the palms of the hands and feet and then spread throughout the body. Xerotic skin, excoriated lesions, and pruritic nodules were seen in the patient. The serum transaminase concentration that should be elevated in this case is normal. CKD is suspected to be the cause. Serum aminotransferase concentrations in patients with chronic kidney disease and chronic dialysis are most often within the lower limits of the normal range.¹² The exact cause is unknown, possibly related to deficiency of pyridoxine phosphate (a coenzyme required for ALT and AST) or the presence of inhibitors in the uremic setting. Complaints of pruritus improving after parturition were assessed based on the decrease in VAS pruritus from moderate to mild (VAS 6 to 2). Based on these data, the diagnosis of ICP can be established.

Management of ICP needs to weigh the benefits with risks to mother and baby due to side effects due to treatment. Pregnant women with ICP are recommended to give birth at 36 weeks to minimize the risk to the fetus. Administration of ursodeoxycholic acid (UDCA) in cases of ICP is recommended as first-line therapy. UDCA is relatively safe and well-tolerated in pregnancy.

Several clinical studies have reported that treating UDCA at a dose of 10-20 mg/kg/day found relief of pruritus, reduced bile acid levels, and improved fetal condition. The mechanism of UDCA works by increasing the excretion of bile acids and other hepatotoxic substances, reducing the risk of fetal morbidity and itching. Topical administration of emollients is included in the treatment options in addition to systemic and non-medical therapy. The use of topical emollients is considered safe and has mild anti-pruritic properties.^{1,4,13} Therapy, in this case, was given topical emollients with the aim of moisturizing dry skin that occurs during pregnancy. The patient has not been treated with UDCA because one week after examination, the patient gave birth.

Perinatal complications associated with ICP include an increased risk of prematurity, intrapartum fetal distress, and stillbirth.^{3,4} The increased risk of fetal death in the womb is 3 to 5 times. A 53-year systematic review found only 14 cases of stillbirth associated with ICP. The frequency of stillbirths in ICP is relatively low at 3 to 10 per 1000 births in the general population.¹ The most extensive prospective observational study from Sweden identified 693 cases of ICP among 45,485 pregnancies and reported a 1-2% increase in the risk of spontaneous preterm delivery, asphyxia, or fluid delivery. The amniotic fluid contains meconium.¹³

Increased maternal bile acid levels can lead to failure of pulmonary surfactant formation. High levels of bile acids can also cause an increase in oxytocin activity so that preterm labor occurs. Low birth weight is caused by chorionic venous vasoconstriction, and placental oxidative stress can even cause the fetus to die in the womb.¹¹ The baby, in this case, was born prematurely and had asphyxia because lung maturation had not

yet occurred. The baby's birth weight is also deficient, increasing the risk of hypothermia.

Conclusion

Pruritus with or without skin changes in the last trimester of pregnancy should consider the possibility of ICP. However, the diagnosis of ICP in CKD patients is biased because they have average or lower serum aminotransferase values. Therefore, strict monitoring of the fetus is vital.

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