

Introduction

Sickle Cell Intrahepatic Cholestasis (SCIC) is an extreme variant of sickle cell disease with high fatality rate. It is observed mainly in patients with homozygous sickle cell anemia. SCIC was first described in 1953 with few cases reported to date, roughly 50% of which were fatal. Here we described a case of SCIC in pregnancy.

Case Report

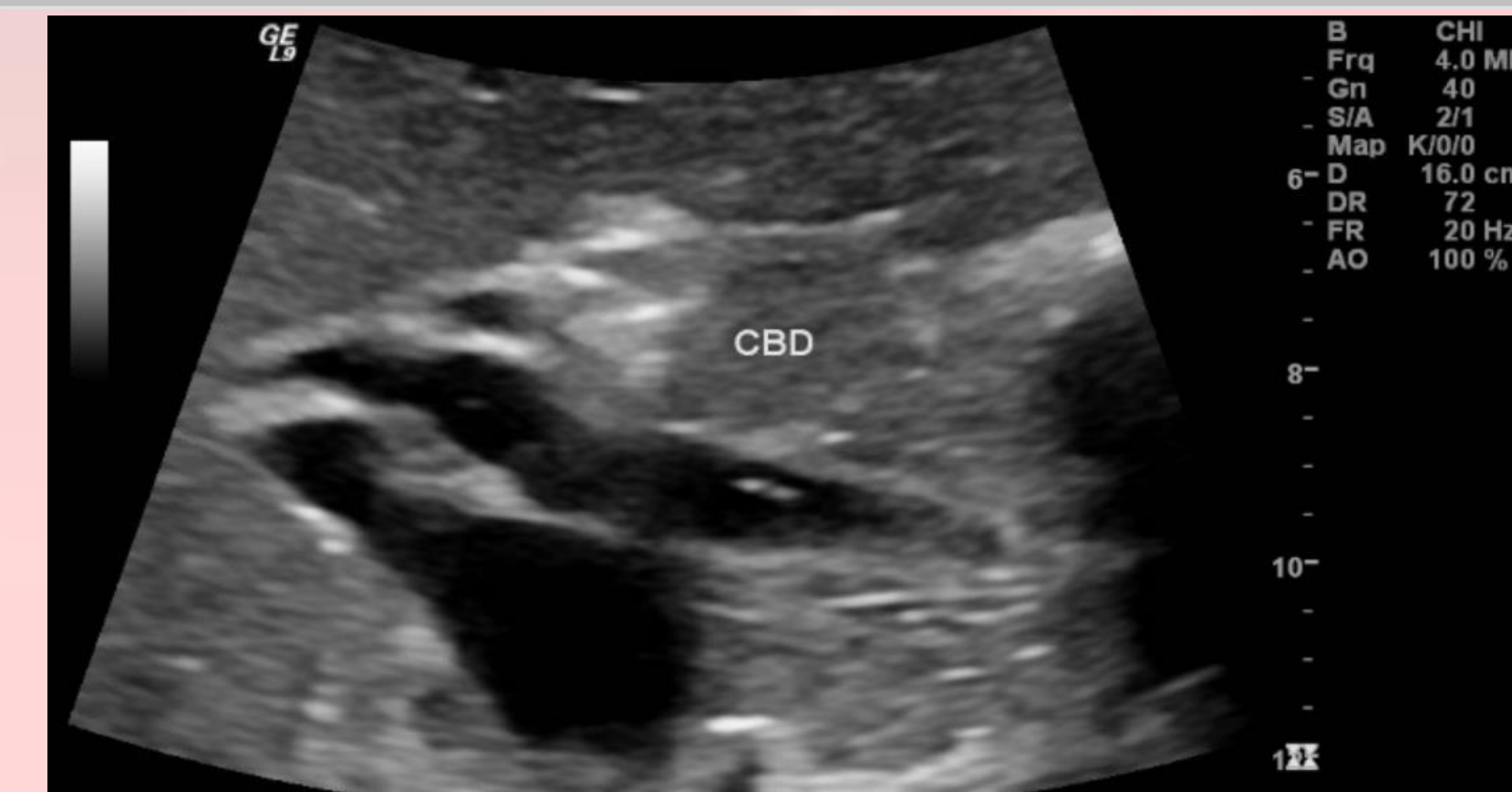
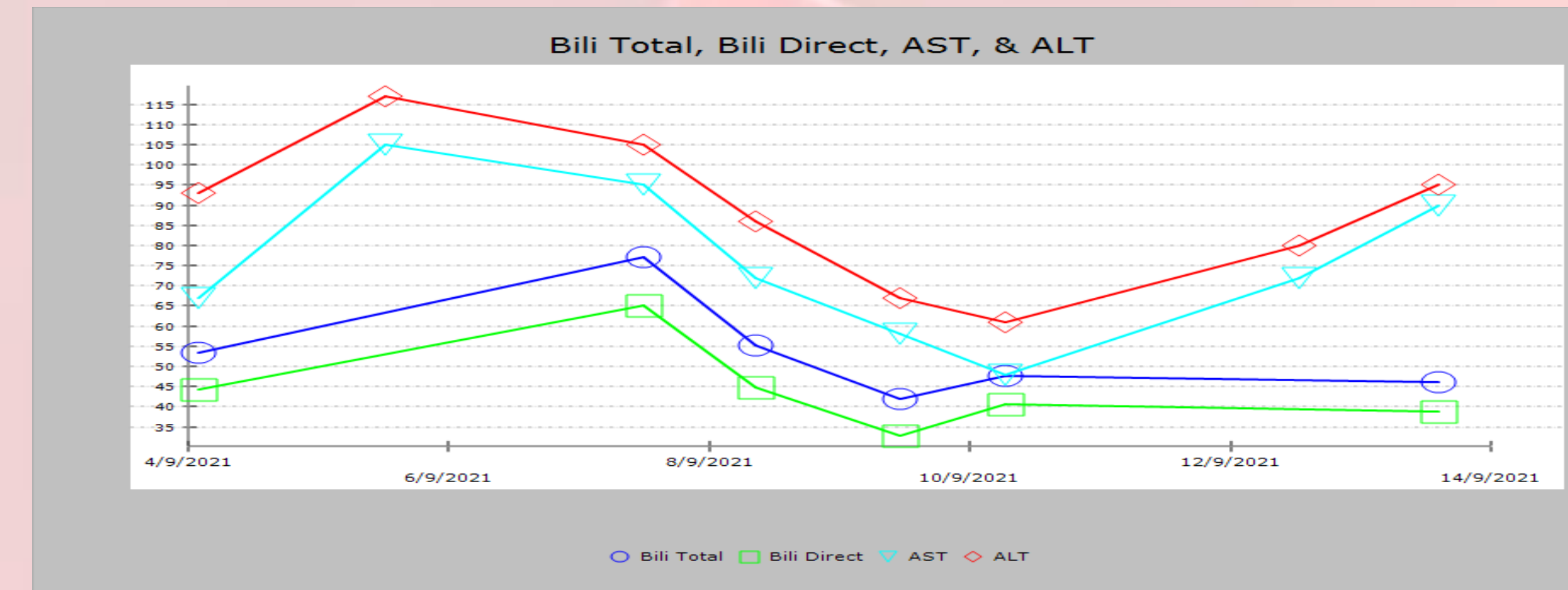
A 24 years old, primigravida, spontaneous conception with known sickle cell disease on regular blood transfusion. Presented at 34 weeks of gestation complaining of lower abdominal pain and fever, which started 2 days ago with worsening of jaundice. She had no urinary or bowel symptoms. History of cholecystectomy 10 years ago. Her parents are sickle cell carrier. She was on Folic acid 5mg OD, Prophylactic Erythromycin 250 mg BD, Aspirin 75mg OD, Enoxaparin 40 mg daily in view of porta cath. She was also on Deferasirox in view of **high ferritin level >8000 mcg/L**, after discussing the benefits and risks with the patient by the haematologist. It was discontinued at 28 weeks of gestation due to noncompliance and no significant drop in the ferritin level. She had COVID infection during early gestation requiring hospitalization as well as urinary tract infection with Klebsiella pneumonia at 15 weeks of gestation which was treated. She also had multiple visits to ER with painful crisis requiring hospitalization and multiple blood transfusion. Her booking investigations were normal except low hemoglobin 7.5 mg/dl. She was Rhesus positive with negative antibody screening. Her glucose tolerance test and thyroid function test were also normal. She had regular growth scan which were normal. Multidisciplinary referral with cardiology, pulmonology to screen for end organ damage and infectious disease for vaccination were done but the patient didn't attend.

On examination she was afebrile, icteric, other physical examination were unremarkable. Urine dipstick was positive for nitrite. On admission the labs were as follows hemoglobin : 8, WBC: 11, retic count : 462 , retic% : 18. Elevated (CRP : 37, AST : 105 , ALT : 117 , Total bilirubin: 53, Direct bilirubin: 44), serology for hepatitis B, C and HIV were negative. Abdominal ultrasound revealed hepatosplenomegaly around 23 cm. Urinary bladder showed debris. **The impression was sickle crisis with urinary tract infection which was managed with IV antibiotics and blood transfusion.**

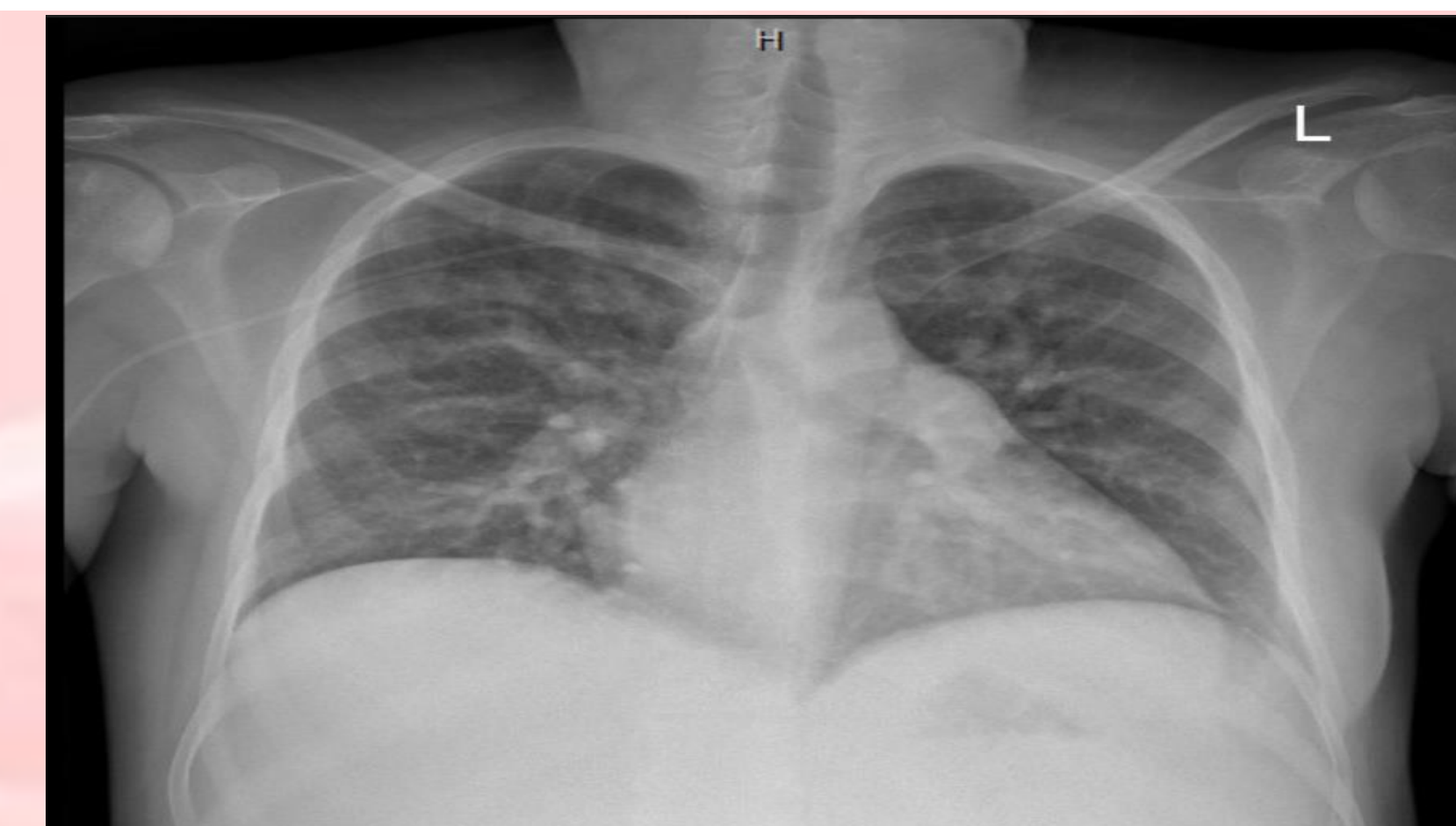
Hospital Course

During the course of the stay, she started to desaturate (92%) and was kept on 2L of oxygen, she also started complaining of itching mainly on the palm/soles and right upper quadrant pain, repeat LFTs were trending downwards however the bile acids were elevated to 36 mmol/L. A multidisciplinary meeting was initiated and the patient was reviewed by the hematologist, gastroenterologist and cardiologist. She received 5 units of blood transfusion. Ultrasound hepatobiliary and doppler demonstrated **Hepatosplenomegaly, the liver measuring 26 cm and the spleen 17 cm with no definite focal lesion and hepatic vein flow was monophasic. The gallbladder was absent, CBD dilated with sludge.** US doppler of lower limbs were normal. ECHO was normal apart from mild mitral regurgitation. She was managed as intrahepatic cholestasis and commenced on Ursodeoxycholic acid (UDCA). Despite being on UDCA the LFTs were elevated along with an increased need of analgesia. In view of crisis pain, persistent desaturation, and elevated LFTs, decision was taken for induction of labour at 35 weeks of gestation. Because of failed induction of labor she had a cesarean section at 35weeks + 3 days of gestation, estimated blood loss was 800 ml, Outcome : Male baby, 2.7 kg, with good APGAR. Patient had uneventful postnatal recovery.

Investigations



CBD dilated with sludge



Mild increase in pulmonary congestion bilaterally.

Discussion

SCIC is mainly a clinical diagnosis. This syndrome is characterized by upper right quadrant pain, enlarged liver, acholic or light stools, marked hyperbilirubinemia, variable elevation of aminotransferases levels, but usually no more than 1–3 times normal. Its presentation ranges from a benign hyperbilirubinemia to a fulminant hepatic failure. Early recognition of this entity is essential to avoid life-threatening complications.

The etiology of intrahepatic cholestasis remains unknown, but it is believed that the deformed erythrocytes adhere to the hepatic vascular endothelium resulting in sludging and congestion of vascular beds, followed by tissue ischemia, infarction, and liver dysfunction in the more severe cases. Diagnosis can be challenging given the overlap in clinical presentation with other conditions affecting the hepatobiliary biliary system in sickle cell anemia such as hepatitis, cholecystitis, and hepatic crisis. According to Ahn et al., SCIC can be subdivided as mild (average direct bilirubin 27.6 mg/dL) and severe diseases (average direct bilirubin 76.8 mg/dL or presence of change in mental status or coagulation disorder), with the death rates being 4% and 64%, respectively. Treatment patterns are not well established and range from supportive care to exchange transfusion. However, early recognition of severe cases and **aggressive exchange transfusion of red blood cells (RBCs) are considered crucial to attain a favorable outcome.**

Conclusion

Exchange transfusion(ET) is the first-line management, due to successful outcomes in the available literature. In the acute setting, simple transfusion in resource-poor environments as a bridge to exchange transfusion is recommended. If ET given early in the disease course significantly improves outcomes of SCIC reversal. It has been proposed to maintain HbS levels < 30%.

References

- Ahn H, Li CS, Wang W. Sickle cell hepatopathy: clinical presentation, treatment, and outcome in pediatric and adult patients. *Pediatr Blood Cancer*. 2005;45:184–90.
- Darakhshan Sohail Ahmed, MBBS¹, Catherine A. McNulty, MD², Muhammed G. Nathani, Sickle Cell Intrahepatic Cholestasis: "A Problem in Disguise"
- Awaad MO, Bayoumi R. Sickle cell disease in adult Bedouins of Al-Ain district, United Arab Emirates. *Emirates*.
- Management of sickle cell disease in pregnancy – Green Top Guidelines
- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3065851/>
- <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5457482/>