Inspissated Bile Syndrome Secondary to G6DP Deficiency in A Tertiary Care Hospital

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Received : August 07, 2026
Published **:** September 04, 2026

ABSTRACT

Introduction: IBS is described as an obstruction of the extrahepatic duct by a bile plug, sludge without bile duct malformation, congenital bile chemical abnormalities, or hepatocellular lesions. It is a relatively rare cause of cholestatic jaundice in infancy.

Case Report: A case of a 15-day-old female brought to the outpatient department with complaints of yellowish discoloration of the skin since birth and a history of meconium staining at birth. On investigation, her hemoglobin, total, and direct bilirubin levels came out to be abnormal, with a G6PD of 0.5 mIU/Ml, abnormal total and direct bilirubin levels and positive coombs test. Ultrasound abdomen showed a partially contracted gallbladder with a CBD of 1.3 mm. Following the confirmation of G6PD deficiency, a diagnosis of inspissated bile syndrome secondary to G6PD was made. Along with her ongoing medication, oral ursodeoxycholic acid was added to her regimen. The patient was discharged on meropenem and vancomycin, on the follow-up day, ultrasonography showed a significant reduction in the CBD's diameter. The patient's serum bilirubin levels, haemoglobin, and other biochemical levels returned to normal.

Discussion: Neonatal jaundice is a common symptom that is often caused by a physiological process. However, conjugated hyperbilirubinemia caused by physical or functional occlusion of the extrahepatic bile duct necessitates immediate diagnostic evaluation and therapy. A 15-day-old female weighing 2.9 kg, born at term to a 28-year-old multiparous female with a history of meconium staining at birth, was brought to the outpatient department with complaints of yellowish discoloration of the skin for 2 weeks. Upon investigation, inspissated bile syndrome secondary to G6DP deficiency was diagnosed, was treated conservatively, and got positive results.

DOI : https://doi.org/10.35702/cases.10030

Conclusion: IBS secondary to HDN accounts for 8% of all types of surgical jaundice during infancy. In some cases, ursodeoxycholic acid (UDCA) appears to be a safe and effective treatment for IBS. However, the possibility of omega-3 PUFAs as a choleretic agent for IBS can also be used as an alternative to surgical intervention. Adjuvant serum changes before, during, and after therapy for IBS could provide additional visual information about the intensity of hemolysis and the efficacy of UDCA. Moreover, prompt diagnosis and use of basic to advanced imaging modalities and investigations are important for early detection and decreasing complications.

Keywords: Meconium Stanning, Coombs Test, Ursodeoxycholic Acid

INTRODUCTION

About 1 in 175,000 infants have inspissated bile syndrome, an uncommon type of cholestatic jaundice [1], which is brought on by biliary sludge obstructing the biliary ducts and gallbladder [2]. Several risk factors have been associated with the production of biliary sludge in infancy, including preterm birth, parenteral feeding, dehydration, haemolytic disorders, cystic fibrosis, congenital heart problems, and sepsis [3]. Because of the physiologic changes that take place during this period, evaluating haemolytic anemia in a baby may be challenging [4]. However, the main complication linked to G6PD deficiency is haemolytic anemia, which in certain cases can be fatal. Glucose-6-phosphate dehydrogenase (G6PD) deficiency is the most prevalent enzymopathy, affecting about 400 million individuals globally. G6DP deficiency manifests as tachycardia, tachypnea, back discomfort, exhaustion, and jaundice. Laboratory results include low haemoglobin and red blood cell counts, reticulocytosis, and elevated unconjugated bilirubin levels [5].

CASE PRESENTATION

A 15-day-old female weighing 2.9 kg, born at term to a 28-year-old multiparous female with a history of meconium staining at birth, was brought to the outpatient department with complaints of yellowish discoloration of the skin for 2 weeks. Before presenting to our facility, on the third day of her birth, she was admitted to the NICU for 5 days with the same complaints and was treated with phototherapy, IV fluids, and a course of IV antibiotics. She also received two packed cell transfusions of O-negative blood during that admission.

On examination, she was afebrile; her pulse was 174 beats per minute; her respiratory rate was 36 breaths per minute; her blood pressure was 82/53 mmHg with a normal centile; her oxygen saturation was 86% at room air and 98% on 2 liters of oxygen via nasal cannula; her capillary refill was more than 3 seconds; and her random blood sugar was 90 mg/dl.

On further examination, she was pale and lethargic, having jaundice involving the palms and soles of her feet with brisk tendon reflexes. The sucking reflex was poor, with an incomplete Moro reflex; the grasp reflex was absent, and the startle reflex was unable to be elicited because of hypertonia. The anterior and posterior fontanels were open, along with visible sutures of the skull. For anthropometry, height was at the 75th percentile, weight at the 25th percentile, and head circumference was at the 25th percentile. On abdominal examination, the liver was palpable 3 cm below the right subcostal margin, with a liver span of 9 cm. The CNS examination was not up to date, along with arching of the body. The respiratory, cardiovascular, and genital examinations were unremarkable.

After sending initial labs of CBC, liver function test, reticulocyte count, and Coombs test, an initial diagnosis of haemolytic disease of newborns with jaundice was established. She was initially managed with the first-line antibiotics meropenem and vancomycin as an empirical treatment, and one packed cell was transfused after cross-matching. She was breastfed and mixed bottle-fed during her treatment.

Clinical laboratory investigations showed a normocytic normochromic RBC morphology with a normal platelet count (418 x 10E9/L). C-reactive protein levels were elevated, measuring 12.7 mg/L. Haemoglobin level was 2.8 g/dL, RBC count was 0.68 x 10E12/L, and NRBC was 09/100 WBC. Abnormal total and direct bilirubin levels were observed. The Coombs test was positive. TSH tests were performed to rule out hypothyroidism, but the results were normal. (Table 1).

Table 1: An initial investigation of ABGs, electrolytes, LFTs, and clinical chemistry

Ph	7.429 (7.36-7.44)
Pco2	12.3mmHg (35-46mmHg)
Po2	207.3mmHg (85-105mmHg)
Bicarbonates	12 mEq/L (23-28mEq/L)
Urea	30mg/dl (10-50mg/dl)
Creatinine	<0.6mg/dl (0.6-1.5 mg/dl)
Calcium	9mg/dl (8.1-10.4 mg/dl)
Sodium	134 mEq/L (136-149 mEq/L)
Potassium	4.6 mEq/L (3.8-5.2 mEq/L)
Chloride	107 mEq/L (98-107 mEq/L)
Total Bilirubin	27.4 mg/dl (<1.5 mg/dl)
Direct Bilirubin	22.1 mg/dl (<0.3mg/dl)
SGPT	67 IU/L
Alkaline phosphate	412 IU/L (<645 IU/L)
Gamma GT	122 IU/L (7-30 IU/L)
TSH	2.08 uIU/ml (0.7-4.8 uIU/ml)

Further investigation of G6PD was sent because of deranged liver function tests, which showed a value of 0.5 mIU/ml, and abdomen sonography findings show a partially contracted gallbladder with a CBD of 1.3 mm.

Following the confirmation of G6PD deficiency, a diagnosis of inspissated bile syndrome secondary to G6PD was made. Along with her ongoing medication, oral ursodeoxycholic acid was added to her regimen. During her five-day hospital stay, she was transfused with two more packed cells along with two IV immunoglobulins to lower down direct bilirubin.

The clinical investigation was repeated on the third day and on the day of her discharge, which showed improvement (Table 2).

The patient was discharged on meropenem and vancomycin with instructions to continue medications for 5 more days and return for follow-up. On the follow-up day, ultrasonography showed a significant reduction in the CBD's diameter. The patient's serum bilirubin levels, haemoglobin, and other biochemical levels returned to normal.

Table 2: The clinical investigation report on the third day and on the day of her discharge

	Third day	**Day of discharge**	**Normal values**
Heamoglobin	7.1 gm/dl	9.9 gm/dl	*12-20 gm/dl*
RBC	2.83 x 10E9/L	3.7 x 10E9/L	*3.6-6.2 x 10E9/L*
Total bilirubin	14.6 mg/L	8 mg/L	*<1.5 mg/dl*
Total bilirubin	9.8 mg/L	6 mg/L	*<0.3 mg/dl*
C-reactive protein	9.5 mg/L	5 mg/L	*Up to 5 mg/L*

DISCUSSION

Neonatal jaundice is a common symptom that is often caused by a physiological process. However, conjugated hyperbilirubinemia caused by physical or functional occlusion of the extrahepatic bile duct necessitates immediate diagnostic evaluation and therapy. Over 90% of extrahepatic bile duct blockages are caused by biliary atresia, making it the most prevalent cause. One unusual cause is a bile stone, sludge, or blockage. The symptoms of inspissated bile syndrome (IBS) include hepatocellular lesions, bile plugs, sludge without bile duct deformity, or congenital bile chemical abnormalities that obstruct the extrahepatic channel.

Blood transfusions, prolonged parenteral feeding, or diuretics are typically the causes of this inspissation and precipitation of

bile and mucus inside the bile ducts [6]. In our case, we found a glucose-6-phosphate dehydrogenase (G6PD) impairment, which is one of the rare causes of IBS. Inspissated bile (IB) syndrome is a rare cause of neonatal cholestatic jaundice, with an approximate incidence of 1 in 175,000 [2].

IBS, first described in 1935, is diagnosed based on a medical history and typical ultrasound features. The incidence in England is 1 in 175,000 live births, accounting for about 8% of all cases of surgical jaundice during infancy [7]. Biliary blockage causes jaundice, pale stools, and dark urine in infants [7].

IBS is diagnosed based on clinical symptoms and ultrasound findings, which include a dilated extrahepatic bile duct, biliary sludge or plugs, and a swollen gall bladder. However, some patients show equivocal or even normal findings. Blood tests reveal elevated AST, ALT, and direct bilirubin levels [6]. In our case, raised serum bilirubin levels and liver enzymes, in conjunction with clinical presentation, are indicative of the findings of previous studies. However, the gallbladder was partially contracted in our case. Long-term fasting, prolonged TPN, hemolytic anemia, hepatitis, transfusion, and the use of antibiotics such ceftriaxone or Diflucan are among the reasons of biliary blockage without structural abnormalities [2].

In our case, transfusion and IV antibiotics could have caused IBS, but since G6DP levels have significantly decreased to a value of 0.5 mIU/ml, IBS secondary to G6PD deficiency was ascertained. Surgical drainage or cholecystostomy drain insertion are examples of conventional therapeutic approaches. Both can be associated with complications and prolonged admissions [2].

IBS treatment might range from hydration to the implantation of an ultrasound-guided percutaneous cholecystostomy drain catheter to physically drain the sludge [8]. Biliary sludge has been known to clear on its own in a few documented cases, either with or without UDCA therapy. Surgical intervention is indicated when the bile duct is dilated to >3 mm with persistent jaundice. Berger et al. documented clinical experience of successfully managing a 6-week-old infant with IBS with laparoscope-aided cholecystostomy with biliary duct lavage [9]. However, in our case, inspissated bile resolved spontaneously through ursodeoxycholic acid (UDCA) and IVIG, with no surgical intervention needed. Upon follow-ups, there was a continual, significant improvement in biochemical results. Ursodeoxycholic acid (UDCA) protects cholangiocytes against the cytotoxicity of hydrophobic bile acids, stimulates hepatobiliary secretion, and protects hepatocytes against bile acid-induced apoptosis. Our case further illustrates that UCDA is an effective treatment consideration for IBS [8].

The majority of cases with spontaneous resolution improved rapidly after one week and did not need a liver biopsy for diagnosis [6].

In one case, omega-3 polyunsaturated fatty acids were utilized instead of surgery. In some medical trials, the use of UDCA alone to dissolve the bile sludge failed to improve biochemical test results, and ultimately, surgery was required. Usually, surgical treatment is only required in cases when the extrahepatic bile ducts have a dilation of greater than 3 mm. With newborns, percutaneous transhepatic cholangiography is one of the most challenging surgical procedures due to the small intrahepatic gall ducts. Failure of the treatment will necessitate a laparotomy for drainage of the inspissated bile [7].

CONCLUSION

IBS secondary to HDN accounts for 8% of all types of surgical jaundice during infancy. In some cases, ursodeoxycholic acid (UDCA) appears to be a safe and effective treatment for IBS. However, the possibility of omega-3 PUFAs as a choleretic agent for IBS can also be used as an alternative to surgical intervention. Adjuvant serum changes before, during, and after therapy for IBS could provide additional visual information about the intensity of hemolysis and the efficacy of UDCA. Moreover, prompt diagnosis and use of basic to advanced imaging modalities and investigations are important for early detection and decreasing complications.

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