
An Infant with Persistent Jaundice and a Normal Newborn Direct Bilirubin Measurement

Sanjiv Harpavat,^{1*} Sridevi Devaraj,^{1,2} and Milton J. Finegold^{1,2}

¹ Department of Pediatrics and; ² Department of Pathology, Baylor College of Medicine and Texas Children's Hospital, Houston, TX.

* Address correspondence to this author at: Clinical Care Center 1010, 6701 Fannin St., Houston, TX 77030. Fax 832-825-3633; e-mail harpavat@bcm.edu.

CASE DESCRIPTION

A 54-day-old infant of Asian descent presented with jaundice. He first started appearing yellow a few weeks after birth. His pediatrician initially recommended increasing sunlight exposure. At subsequent visits, the pediatrician recommended stopping breastfeeding. Despite these interventions, the infant's jaundice persisted and his stools became pale. At 52 days of life (DoL), he had a serum bilirubin measured, and the reported "Bilirubin, Direct" concentration of 5.54 mg/dL (reference interval, 0.0–0.4 mg/dL) prompted an immediate referral (see Table 1 for a summary of laboratory results).

The infant's physical examination and evaluation results were most consistent with biliary atresia (BA). He had marked jaundice, with a reported "Bili Conjugated" of 4.7 mg/dL (reference interval, 0.0–0.2 mg/dL), as well as increased aspartate aminotransferase, alanine aminotransferase, and γ -glutamyltransferase activities. He otherwise appeared well and had 2 newborn screens with results within reference intervals, making infectious or metabolic etiologies unlikely. Furthermore, protease inhibitor typing, chest radiograph, and abdominal ultrasound revealed no abnormalities, arguing against other liver-associated causes such as α_1 -antitrypsin disease, Alagille syndrome, and choledochal cyst.

There was one laboratory result, however, that was inconsistent with BA: his newborn conjugated bilirubin concentration, reported as "Neonatal Dbil." In our experience, infants with BA have newborn direct or conjugated bilirubin concentrations that exceed their birth hospital's derived reference interval (1). In contrast, this infant had a reported "Neonatal Dbil" concentration of 0.5 mg/dL on DoL 1, which was within the birth hospital's reported reference interval of 0.0–0.6 mg/dL. The bilirubin was measured using a Vitros analyzer, and the reference interval was derived by the manufacturer based on "40 apparently healthy neonates" (2).

Because infants with BA treated earlier have the best outcomes, we continued the evaluation despite the discrepant newborn bilirubin concentrations. He promptly underwent liver biopsy, which showed fibrosis and bile duct proliferation characteristic of BA. Subsequent intraoperative cholangiogram confirmed the BA diagnosis. However, one important question still remained: how could the infant's reportedly normal "Neonatal Dbil" concentration at birth be explained?

References

1. Harpavat S, Finegold MJ, Karpen SJ. Patients with biliary atresia have elevated direct/conjugated bilirubin levels shortly after birth. *Pediatrics* 2011;128:e1428–33.
2. Ortho-Clinical Diagnostics. Instructions for use: VITROS chemistry products BuBc slides (bilirubin, unconjugated and conjugated). Version 6.0. Rochester (NY): Ortho-Clinical Diagnostics, Inc.; 2012.

Questions to Consider

- What is the difference between “Neonatal Dbil,” “Bilirubin, Direct,” and “Bili Conjugated”?
- How should reference intervals be established?
- Why are the reference intervals for the 3 tests in Table 1 different?

Table 1. Summary of fractionated bilirubin results.

Day of life	Test name	Assay	Instrument	Result, mg/dL	Reference interval, mg/dL	Reference interval source
1	“Neonatal Dbil”	Direct spectrophotometry	Vitros	0.5	0.0–0.6	Manufacturer
52	“Bilirubin, Direct”	Chemical reaction (Diazo)	Roche	5.54	0.0–0.4	Laboratory derived
54	“Bili Conjugated”	Direct spectrophotometry	Vitros	4.7	0.0–0.2	Laboratory derived

Final Publication and Comments

The final published version with discussion and comments from the experts will appear in the February 2015 issue of *Clinical Chemistry*. To view the case and comments online, go to <http://www.clinchem.org/content/vol61/issue2> and follow the link to the Clinical Case Study and Commentaries.

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