

Bile Acids, Fractionated and Total

FOR THE MEASUREMENT OF INDIVIDUAL BILE ACIDS IN SERUM

Test Highlights

- Free acids, glycine conjugates, and taurine conjugates of cholic, deoxycholic, chenodeoxycholic, and ursodeoxycholic acids (ursodiol) are quantified.
- Results for the sum of each bile acid are reported, as well as the overall total.
- Sensitive and specific LC-MS/MS method is employed.
- Small sample volume required (0.2 mL minimum).
- Ursodeoxycholic acid (ursodiol) is included for assessing compliance with therapy.

Clinical Background

- Hepatic clearance of bile acids from portal blood is efficient in normal subjects. Low serum concentrations of bile acid are observed.
- Following meals, serum bile acid levels have been shown to increase only slightly in normal persons, but markedly in patients with various liver diseases, including Budd-Chiari syndrome, cholangitis, cholestasis, cholestasis of pregnancy, cirrhosis, hemochromatosis, hepatitis, portal-vein thrombosis, and Wilson disease.
- Some inborn errors of bile acid metabolism result in very low concentrations of all bile acids. Patients with these diseases respond to therapy with specific bile acids.
- Other inborn errors of bile acid metabolism result in high concentrations of individual bile acids. Patients with these diseases also respond to therapy with specific bile acids.

Disease Overview

- Defective bile acid synthesis:
 - 3 β -hydroxysteroid- Δ 5-oxidoreductase/isomerase deficiency is characterized by jaundice, hepatomegaly, pale stools, and dark urine. No normal bile acids are present in serum.
 - 3-oxo- Δ 4-steroid 5 β -reductase deficiency is another cholestatic disease with similar symptoms. Serum bile acid concentrations are elevated and chenodeoxycholic acid is the predominant species.
- Abnormalities of bile acid delivery to the bowel, including intrahepatic cholestasis and extrahepatic bile duct obstruction, may increase the concentration of cholic acid.
- Interruption of enterohepatic circulation of bile acids may lead to a decrease in serum bile acid concentrations.
- Disturbances of bile acid metabolism in hepatocellular disease may lead to an increase in fasting serum bile acid concentrations and a larger than normal increase in postprandial serum bile acid concentrations.

Epidemiology

Inborn errors of bile acid metabolism are very rare.

Indications for Ordering

- Clinical evidence of an inborn error of bile acid metabolism. This may include evidence of cholestatic liver disease at birth, such as pale stools, dark urine, and progressive jaundice. It may also include hepatic dysfunction with increased serum activities of transaminases and alkaline phosphatase, increased concentrations of conjugated bilirubin, and malabsorption of vitamins D and E.
- May be useful for patients receiving bile acid therapy with chenodeoxycholic acid, cholic acid, or ursodeoxycholic acid (ursodiol).

Interpretation

- Fasting reference intervals for each bile acid and the sum of all are provided. Values may be elevated after a meal.
- In cholestasis, the ratio of cholic acid to chenodeoxycholic acid increases.
- In hepatitis and cirrhosis the ratio of cholic acid to chenodeoxycholic acid decreases.

Limitations

- The current method does not quantify sulfated or glycoside-conjugated forms of bile acids.
- The current method does not measure any form of lithocholic acid. However, lithocholic acid is usually present at low concentrations in serum.
- This assay has only been validated for serum.

Methodology

- Deuterated internal standards are added to the sample and proteins are precipitated.
- Two-dimensional HPLC is performed, followed by electrospray ionization tandem mass spectrometry with negative ion monitoring.

Related Tests

- Bile Acids, Total (0070189)
- Hepatic Function Panel (0020416)

References

1. Barnes S, et al. Diagnostic value of serum bile acid estimations in liver disease. *J Clin Pathol* 1975;28:506–509.
2. LaRusso NF, et al. Dynamics of the enterohepatic circulation of bile acids. *N Eng J Med* 1974;291:689–692.
3. Björkhem I, Boberg KM, Lietersdorg E. Inborn errors in bile acid biosynthesis and storage of sterols other than cholesterol. In *The Metabolic & Molecular Bases of Inherited Disease*, 8th ed. CR Scriver, et al., eds. 2001. New York: McGraw-Hill, 2961–88.
4. Dufour DR. Liver Disease. In *Tietz Textbook of Clinical Chemistry and Molecular Diagnostics*, 4th ed. CA Burtis, ER Ashwood, DE Bruns, eds. 2006; St. Louis: Elsevier Saunders,1782–7.
5. Setchell KDR, et al. Defects in bile acids biosynthesis—diagnosis and treatment. *J Pediatr Gastroenterol Nutr* 2006; 43:S17–22.

Test Information

0092610 Bile Acids, Fractionated and Total by LC-MS/MS

For specific collection, transport, and testing information, refer to the ARUP Web site at www.aruplab.com.

For information on test selection, ordering, and interpretation, refer to ARUP Consult® at www.arupconsult.com.