

TEST ID: 7AC4

7AC4, BILE ACID SYNTHESIS, SERUM

USEFUL FOR

Screening for bile acid malabsorption in patients with irritable bowel syndrome-diarrhea (IBS-D)

CLINICAL INFORMATION

Bile acids are synthesized from cholesterol in the liver and released into the digestive tract where they function to emulsify dietary fats and facilitate lipid absorption in the small intestine. More than 95% of bile acids are then reabsorbed primarily by active uptake in the distal ileum, while less than 5% are excreted in stool. The synthesis of bile acids in the liver is regulated by a negative feedback mechanism from the bile acids reabsorbed from the intestine. 7 Alpha-hydroxy-4-cholesten-3-one (7aC4) is an intermediate in the biosynthesis pathway of cholesterol to bile acids. The concentration of 7aC4 in serum is a surrogate for the amount of bile acid synthesis in the liver. There is some diurnal variation in 7aC4 serum concentrations, so measurement should be performed on a fasting morning sample.

Patients with increased bile acid in their stool suffer from chronic diarrhea termed bile acid diarrhea (BAD). Approximately 10% to 33% of patients with irritable bowel syndrome with primarily diarrhea (IBS-D) have BAD. Identifying patients with BAD can be done by measuring total and fractionated bile acids in stool. The increased bile acids in feces can be caused by an inability to reabsorb bile acids in the terminal ileum (bile acid malabsorption). The loss of intestinal reabsorption leads to increase synthesis of bile acids in the liver. Recent studies have shown that serum concentrations of 7aC4 are elevated in patients with BAD and can be used as a surrogate to the timed fecal collection. Several intestinal diseases or functional abnormalities can lead to BAD. Identification of these patients can influence treatment decisions that could include the use of bile acid sequestrants.

Conversely, patients with IBS with predominately constipation (IBS-C) may have lower circulating 7aC4 as compared to healthy individuals.

INTERPRETATION

In patients with irritable bowel syndrome-diarrhea (IBS-D), elevated 7alpha-hydroxy-4-cholesten-3-one (7AC4) is consistent with bile acid diarrhea (BAD). A result of 17.6 ng/mL or greater is 83% sensitive and 53% specific for BAD. In these cases, a confirmatory 48-hour fecal bile acid test could be considered. A result above the reference interval (>63.2 ng/mL) is 6% sensitive and 92% specific for BAD.

REFERENCE VALUES

≥18 years: 2.5–63.2 ng/mL

Reference values have not been established for patients who are <18 years of age.

ANALYTIC TIME

2 days

SPECIMEN REQUIRED

Type

Serum

Collection Container/Tube

Preferred: Serum gel

Acceptable: Red top

Submission Container/Tube

Plastic vial

Specimen Volume

1 mL

SUPPORTIVE DATA

From an internal study of 55 patients with irritable bowel syndrome-diarrhea (IBS-D), a fasting serum 7 alpha-hydroxy-4-cholesten-3-one (7aC4) result of ≥ 17.6 ng/mL was 83% sensitive and 53% specific for identifying patients with elevated fecal bile acids (eg, patient with BAD). In that same study, a result above the reference interval (>63.2 ng/mL) displayed poor sensitivity (6%) but high specificity (92%) for BAD.

CLINICAL REFERENCE

1. Vijayvargiya P, Camilleri M, Shin A, et al: Methods for diagnosis of bile acid malabsorption in clinical practice. Clin Gastroenterol Hepatol 2013;11(10):1232-1239
2. Camilleri M, Nadeau A, Tremaine WJ, et al: Measurement of Serum 7 Alpha-hydroxy-4-cholesten-3-one (or 7AC4), a Surrogate test for bile acid malabsorption in health, ileal disease and irritable bowel syndrome using liquid chromatography-tandem mass spectrometry. Neurogastroenterol Motil 2009;21(7):734-743
3. Wong BS, Camilleri M, Carlson P, et al: Increased bile acid biosynthesis is associated with irritable bowel syndrome with diarrhea. Clin Gastroenterol Hepatol 2012 Sep;10(9):1009-1015.e3