

## Iron, Ferritin, Transferrin, TIBC

### WHAT IS IRON?

Iron is a mineral with several essential functions in the body. It constitutes the core of both hemoglobin, the molecule that carries oxygen from the lungs to the rest of the body, and myoglobin, a protein that provides oxygen to the muscles. Iron is also essential for growth, normal cell function, and the production of connective tissue and some hormones (1).

### WHAT IS FERRITIN?

Approximately 25% of the iron in a normal adult is present in a storage form (2), with the most common form being ferritin (accounting for about 2/3 of storage iron) (3). Ferritin analyses provide a sensitive, specific, and reliable measurement for determining iron deficiency at an early stage (4), and are also useful for monitoring the reaccumulation of iron stores in iron-deficient individuals who are taking iron supplements.

### WHAT IS TRANSFERRIN AND TRANSFERRIN SATURATION?

Transferrin is the main protein that binds to and transports iron around the body. Transferrin saturation is an estimate of how many of the transferrin iron-binding sites are occupied by iron.

### WHAT IS TIBC?

Total iron binding capacity (TIBC) refers to the total amount of iron that can be bound by proteins in the blood. Transferrin is the primary iron-binding protein; hence the TIBC measurement is a good indirect measurement of transferrin availability. However, TIBC and transferrin are not synonymous.

### REFERENCE RANGES

Healthy iron levels are 65 – 175 µg/dL in males and 50 – 170 µg/dL in females (5).

Healthy ferritin levels are 40 – 300 ng/mL for males and 20 – 200 ng/mL for females (6). Ferritin levels below 10 ng/mL are indicative of iron deficiency anemia, while levels above 200-300 ng/mL may indicate hemochromatosis or other health complications.

Healthy transferrin levels vary slightly by age and gender. 174 - 364 mg/dL is considered normal for adult males aged 14 - 60 years, while the normal range for adult females is 180 - 382 mg/dL. The normal ranges for over 60 years are slightly lower, at 163 - 344 mg/dL (males) and 173 - 360 mg/dL (females) (7).

Average transferrin saturation is 25%, with a normal range of 14 - 50%. Below 10% indicates severe iron deficiency (8), and above 50% indicates iron overload, which can result in organ damage due to toxic non-transferrin bound iron (9).

Normal TIBC values are between 240 and 450 µg/dL (10). Higher TIBC values indicate that the body's iron supplies are low, such as in cases of iron deficiency anemia or late in pregnancy (11). Lower TIBC values can indicate hemolytic anemia (when red blood cells are destroyed too quickly), hypoproteinemia (low blood protein levels), inflammation, liver disease, malnutrition, or sickle cell anemia (12).

### SIGNS OF IRON DEFICIENCY

Low iron levels inhibit the production of hemoglobin, resulting in reduced red blood cells. When the body can't supply enough red blood cells to meet its demands, it manifests as anemia, which affects an estimated two billion people around the globe (13). Symptoms include tiredness, fatigue, pale skin, shortness of breath, headaches, and dizziness. These initial symptoms of deficiency can go unnoticed, but if left untreated, anemia can have serious repercussions, including impaired cognitive function, disturbances in the digestive system, and impaired immunity. Pregnant women, young children and frequent blood donors are at a much higher risk of iron deficiency (14).

### SIGNS OF EXCESS IRON

Increased iron concentrations occur in hemochromatosis and acute liver disease. Usually only 8-10% of iron from the diet is absorbed. However, individuals with hemochromatosis can absorb three to four times more iron than normal (15). This excess iron cannot be naturally excreted from the body, so it accumulates in organs and tissues, eventually causing serious health complications. The symptoms of hemochromatosis include fatigue, joint pain, abdominal pain, memory problems, depression, decreased sex drive, shortness of breath, and heart flutters. Further serious complications can occur in untreated individuals, including heart failure, liver cirrhosis and disease, and endocrine problems (16).

### TEST PROCEDURE

Correct specimen collection and handling is required for optimal assay performance.

This test requires a blood sample from a finger prick. All supplies for sample collection are provided in this kit. First wash and dry hands. Warm hands aid in blood collection. Clean the finger prick site with the alcohol swab and allow to air dry. Use the provided lancet to puncture the skin in one quick, continuous and deliberate stroke. Wipe away the first drop of blood. Massage hand and finger to increase blood flow to the puncture site. Angle arm and hand downwards to facilitate blood collection on the fingertip. Drip blood onto the blood collection card or into the microtainer tube.

Avoid squeezing or 'milking' the finger excessively. If blood flow stops, perform a second skin puncture on another finger, if more blood is required. Do not touch the fingertip.

Dispose of all sharps safely and return sample to the laboratory in the provided prepaid return shipping envelope.

Upon receipt at the laboratory, the blood sample is analyzed by the following fully automated assays on the Alinity ci series analyzer:

- Alinity c Iron
- Alinity i Ferritin
- Alinity c Transferrin

The Transferrin Saturation and Total Iron Binding Capacity (TIBC) values are calculated from the results of the Alinity assays above.

## DISCLAIMERS/LIMITATIONS

Certain medications (e.g., birth control pills and antithyroid medicines), pregnancy, receiving a blood transfusion in the past four months, inflammation due to surgery, injury, or infection, having a radioactive scan in the past three days, and reduced kidney function can affect complete iron panel results.

These results should be interpreted in conjunction with other laboratory and clinical information.

Additional testing is recommended if iron levels are inconsistent with clinical evidence.

Correct specimen collection and handling is required for optimal assay performance.

Interferences from medication or endogenous substances may affect results.

Chronic inflammatory disorders may interfere with ferritin analyses.

Values obtained with different assay methods should not be used interchangeably in serial testing.

The ferritin assay is not recommended for use during pregnancy, as ferritin diminishes late in pregnancy even when adequate iron stores are present.

False results may occur in specimens from individuals that have received preparations of mouse monoclonal antibodies for diagnosis or therapy.

## REFERENCES

- (1) Bothwell TH, et al. (1989). Nutritional iron requirements and food iron absorption. *J Int Med.* 226(5), 357-365.
- (2) Krause JR, Stolc V. (1979). Serum Ferritin and Bone Marrow Iron Stores. Correlation with Absence of Iron in Biopsy Specimens. *Am J Clin Pathol.* 72, 817-820.
- (3) Skikne BS, Cook JD. (1981). Serum Ferritin in the Evaluation of Iron Status. *Lab Management.* 19, 31-35.
- (4) Bates HM. (1980). How to Detect Iron Deficiency Before Anemia Develops. *Laboratory Pathfinder.* Jan 1980:17-22.
- (5) Tietz NW, editor. *Clinical Guide to Laboratory Tests*, 4th ed. St. Louis, MO: Elsevier Saunders; 2006:634-635.
- (6) Camaschella C. Iron-deficiency anemia. *N Engl J Med.* 2015 May 7;372(19):1832-43.
- (7) Ritchie RF, et al. (1999). Reference distributions for the negative acute-phase serum proteins, albumin, transferrin and transthyretin: a practical, simple and clinically relevant approach in a large cohort. *J Clin Lab Anal.* 13(6):273-9.
- (8) Bermejo F, García-López S. (2009). A guide to diagnosis of iron deficiency and iron deficiency anemia in digestive diseases. *World J Gastroenterol.* 15(37), 4638-4643.
- (9) Mainous AG, Gill JM, Carek PJ. (2004). Elevated Serum Transferrin and Mortality. *Ann Fam Med.* 2(2), 133-138.
- (10) Faruqi A and Mukkamalla SKR. (2020). Iron Binding Capacity. *StatPearls [Internet]*. Treasure Island (FL).
- (11) Chernecky CC, Berger BJ. (2013). Iron (Fe) and total iron-binding capacity (TIBC)/transferrin – serum. In: Chernecky CC, Berger BJ, eds. *Laboratory Tests and Diagnostic Procedures*. 6th ed. Philadelphia, PA: Elsevier; 2013:691-692.
- (12) Brittenham GM. (2018). Disorders of iron homeostasis: iron deficiency and overload. In: Hoffman R, Benz EJ, Silberstein LE, et al, eds. *Hematology: Basic Principles and Practice*. 7th ed. Philadelphia, PA: Elsevier; 2018:chap 36.
- (13) Zimmermann MB and Hurrell RF. (2007). Nutritional iron deficiency. *The Lancet.* 370(9586), 511-520.
- (14) Camaschella C. (2015). Iron-Deficiency Anemia. *N Engl J Med.* 372, 1832-1843.
- (15) Witte DL, et al. (1996). Hereditary hemochromatosis. *Clinica Chimica Acta.* 245(2), 139-200.
- (16) Beutler E, Felitti V, Gelbart T, Ho N. (2001) Genetics of Iron Storage and Hemochromatosis. *Drug Metab Dispos.* 29(4):495-499.