NxGen MDx

HBB-Related Hemoglobinopathies (Beta-Thalassemia/Sickle Cell Disease)

What Your Results Mean

Test results indicate that you are a carrier of an *HBB*-related hemoglobinopathy (beta-thalassemia/sickle cell disease). Carriers may experience mild anemia that typically does not require additional management. You and your partner or donor would both have to be carriers of an *HBB*-related hemoglobinopathy for there to be an increased chance to have a child with symptoms; this is known as autosomal recessive inheritance. Different variations within the *HBB* gene can cause different conditions, such as beta thalassemia or sickle cell disease. Carrier testing of your partner or donor is recommended in addition to consultation with a genetic counselor for a more detailed risk assessment.

We recommend that you share and discuss this information with all of your health care providers. Since this is an inherited gene change, this information may be helpful to share with family members as it may impact their family planning and their own personal clinical management.

Recommended Next Steps

Carrier testing of your partner or donor is recommended in addition to consultation with a genetic counselor for a more detailed risk assessment. If both you and your partner or donor are carriers for an HBB-related hemoglobinopathy, each of your children has a 1 in 4 (25%) chance to have the condition. Reflexive testing for the *HBA1/2* genes, causative of alpha thalassemia, may be considered if you are a carrier of beta thalassemia to assess the risk of having a child with an alpha/beta globin chain imbalance.

HBB-Related Hemoglobinopathies (Beta-Thalassemia/Sickle Cell Disease) Explained

What are HBB-Related Hemoglobinopathies (Beta-Thalassemia/Sickle Cell Disease)?

Beta thalassemia is an inherited disorder that affects red blood cells. Beta thalassemia major is a lifelong condition characterized by severe anemia, mild jaundice (yellowing of the skin and whites of the eyes), skeletal changes in the face, and an enlarged spleen and liver. Individuals with beta thalassemia major are typically diagnosed early in childhood. Beta thalassemia intermedia is a milder form and signs and symptoms are similar to beta thalassemia major, but it is less severe and may be diagnosed later in adulthood. Beta thalassemia due to an alpha/beta-globin imbalance has similar symptoms to beta thalassemia intermedia.

Sickle cell anemia is an inherited disorder that affects the red blood cells, creating a crescent or sickle shape of the red blood cells. The abnormal red blood cells can clog blood vessels, preventing delivery of oxygen to tissues and organs, causing the symptoms of the disease. Sickle cell anemia is a lifelong condition characterized by painful episodes, anemia, organ damage, infections, lung problems, leg ulcers, bone damage, and strokes.

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Hemoglobin E is caused by a specific variant in the *HBB* gene, which encodes the beta-globin subunits. Individuals with hemoglobin E disease are typically asymptomatic, but may have mild to moderate anemia, slight reduction in red blood cell survival, and occasional splenomegaly. The most clinically significant hemoglobin E disorder is hemoglobin E/beta-thalassemia. This occurs when hemoglobin E trait is inherited with beta-thalassemia. Symptoms of this disorder include moderate to severe hemolytic anemia, very low MCV, increased reticulocyte count, heart failure, splenomegaly, hepatomegaly, and poor growth.

Hemoglobin C disease is caused by a specific variant on the *HBB* gene, which encodes the beta-globin subunits. Individuals with one *HBB* gene variant (hemoglobin C trait) do not typically have related health problems, although they may have a slightly low mean corpuscular volume (MCV). However, when hemoglobin C trait is inherited with other hemoglobinopathies, it may have clinical significance. Individuals with hemoglobin C disease may experience mild hemolytic anemia, particularly when under stress. They may also experience splenomegaly, jaundice and/or gallstones. Overall, hemoglobin C disease is considered a mild disorder with a normal life expectancy.

Prognosis

Prognosis is dependent on the type of hemoglobinopathy and the severity of symptoms. Typically, prognosis for beta thalassemia is fair with regular blood transfusions and chelation therapy. Individuals with beta thalassemia typically live to their third or fourth decade of life.

Prognosis for sickle cell anemia is also considered fair with treatment. Affected individuals live up to their fourth to sixth decade of life. Individuals with hemoglobin C or E disease generally have a good prognosis, as many may be asymptomatic.

Treatment

Management of beta thalassemia major includes regular blood transfusions as well as chelation therapy to prevent iron overload. Without transfusion and proper treatment, beta thalassemia disease can be fatal within the first two years of life. Stem cell transplantation is curative; however, difficulty identifying matched donors has proven to be a barrier to transplantation.

Management of sickle cell disease is generally focused on good hydration, avoidance of extreme temperatures and fatigue, and pain management. Prophylactic penicillin is recommended in childhood to reduce the risk of infection. Hydroxyurea has been shown to decrease painful episodes and increase life span. Individuals with the disease may require joint replacement, hemodialysis, kidney transplantation, splenectomy, cholecystectomy, red blood cell exchange transfusion for strokes, and other treatments for symptoms of the disease. Like with beta thalassemia, stem cell transplantation is curative; however, difficulty identifying matched donors has proven to be a barrier to transplantation.

Resources
Cooley's Anemia Foundation
http://www.cooleysanemia.org/
American Sickle Cell Anemia Foundation
http://www.ascaa.org/
National Organization for Rare Disorders (NORD)
https://rarediseases.org/rare-diseases/thalassemia-major/
https://rarediseases.org/rare-diseases/sickle-cell-disease/
National Society of Genetic Counselors
https://www.nsgc.org/

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