Alpha-Thalassemia/ Alpha-Globin Triplication

What Your Results Mean

Alpha-Thalassemia

There are two types of alpha-thalassemia carriers: alpha-thalassemia silent carriers and alpha-thalassemia trait carriers. Individuals who are silent carriers of alpha thalassemia are not expected to show symptoms. Individuals with alpha thalassemia trait may be identified to have mild anemia in the presence of normal iron levels. Individuals with alpha-thalassemia trait typically do not require any medical management or treatment. You and your partner would both have to be carriers of alpha thalassemia to have an increased chance to have a child with symptoms. This is known as autosomal recessive inheritance. Carrier testing of your partner or donor is recommended in addition to consultation with a genetic counselor for a more detailed risk assessment.

Alpha-Globin Triplication

When an individual has more than four alpha-globin genes, this is referred to as an alpha-globin triplication. Extra alpha-globin genes can cause alpha/beta hemoglobin imbalance in the presence of beta-thalassemia or beta-thalassemia trait. Individuals with an alpha-globin triplication without beta-thalassemia or beta-thalassemia trait are not expected to show symptoms. Your partner would have to be a carrier of beta-thalassemia for there to be an increased chance to have a child with symptoms. This is known as autosomal recessive inheritance. 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.

Recommended Next Steps

Alpha-Thalassemia

Carrier testing of your partner or donor is recommended in addition to consultation with a genetic counselor for a more detailed risk assessment. If one parent is an alpha thalassemia carrier, the risk to have a child with any clinical manifestation of the disorder depends on the allele number (copies of *HBA1* and *HBA2*) and allele positioning (cis or trans) of the person's partner. Silent carriers are not at an increased risk to have a child with Hb Bart syndrome.

Alpha-Globin Triplication

Carrier testing of your partner or donor is recommended in addition to consultation with a genetic counselor for a more detailed risk assessment. If your partner is a carrier for beta-thalassemia, each of your children has a 1 in 4 (25%) chance to have beta thalassemia due to alpha/beta hemoglobin imbalance. Your partner's alpha-thalassemia carrier status does not affect the reproductive risk associated with your result, and therefore testing your partner for these genes is not necessary.

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Alpha Thalassemia Explained

What is Alpha-Thalassemia?

Alpha-thalassemia is an inherited disorder caused by decreased synthesis of hemoglobin alpha chain, a protein in the red blood cells required for oxygen delivery. The clinical features of alpha thalassemia can be explained by deletions or variants in the *HBA1* or *HBA2* alpha-globin genes. Typically, individuals have two copies of the *HBA1* and *HBA2* genes, for a total of four alleles encoding for the alpha chain component of hemoglobin in red blood cells. There are two types of alpha thalassemia: Hb Bart syndrome (hydrops fetalis) and HbH disease. In the most severe type, Hb Bart syndrome (0 copies of *HBA1* or *HBA2*), pregnancies may result in stillbirth or early infant death. Anemia, enlargement of the spleen and liver, mild jaundice, and skeletal changes (particularly in the face) are general features of HbH disease (1 copy of *HBA1* or *HBA2*).

What is Beta-Thalassemia Due to Alpha/Beta Hemoglobin Imbalance?

Individuals with more than four alpha-globin genes and beta-thalassemia or beta-thalassemia trait would have a diagnosis of beta-thalassemia intermedia. Beta thalassemia is a blood disorder that reduces the production of hemoglobin. Hemoglobin is the iron-containing protein in red blood cells that carries oxygen to cells throughout the body. As a result, affected individuals have mild to moderate anemia and may also have slow growth and bone abnormalities.

Prognosis

Alpha-Thalassemia

Prognosis of alpha thalassemia depends on which type an individual is diagnosed with. The prognosis of Hb Bart syndrome is poor; it is known to be fatal and can often result in miscarriage or stillbirth. For HbH disease, prognosis is typically fair; however, it depends on the severity of the signs and symptoms which can vary in each individual. If individuals with HbH disease are receiving proper treatment, they can live well into adulthood.

Beta-Thalassemia Due to Alpha/Beta Hemoglobin Imbalance

Prognosis of beta-thalassemia due to alpha/beta hemoglobin imbalance is typically fair, though severity of the signs and symptoms vary in each individual. If individuals with an alpha/beta hemoglobin imbalance are receiving proper treatment, they can live well into adulthood.

Treatment

Alpha-Thalassemia

Management of Hb Bart syndrome is focused on care of the mother during pregnancy as well as supportive care in infancy. Individuals with HbH disease require annual follow up with a hematologist and may require red blood cell transfusions. Other complications such as splenomegaly, gallstones, and leg ulcers may require appropriate medical or surgical treatment.

Beta-Thalassemia Due to Alpha/Beta Hemoglobin Imbalance

The most common treatment for beta thalassemia due to alpha/beta hemoglobin imbalance is blood transfusions, which provide a temporary supply of healthy red blood cells to bring oxygen to the body. If transfusions occur frequently, they may result in a toxic buildup of iron in the blood. To counteract this side effect, individuals with beta thalassemia require chelation therapy, which helps eliminate excess iron from the body.

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Resources
Cooley's Anemia Foundation
http://www.thalassemia.org/
National Organization for Rare Disorders (NORD)
https://rarediseases.org/rare-diseases/alpha-thalassemia/
National Society of Genetic Counselors
https://www.nsgc.org/

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