Editorial

Benefits of Early Diagnosis of Thalassemia in Children

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Introduction

Thalassemia is an inherited blood disorder, which means that it is passed from parents to children through genes.

If you have thalassemia, your body may not make enough hemoglobin, which can lead to fewer healthy red blood cells. This can lead to a condition called anemia.

Anemia can make you feel tired, weak, or short of breath. Or, depending on the type of thalassemia you have and how serious it is, you may have no symptoms at all. More serious types of thalassemia are usually diagnosed before a child is 2 years old.

Blood transfusions are used to treat thalassemia. You may need occasional or more regular blood transfusions, depending on how serious your condition is. You may also take medicine to help with complications from this treatment. It is important to talk to your healthcare provider before you become pregnant. They may need to run tests or change your treatment plan.

Although thalassemia is a lifelong condition, treatments have improved over the years. People are now living with thalassemia for longer and have better quality of life.

Types of Thalassemia

There are two main types of thalassemia: alpha thalassemia and beta thalassemia. Each of these types can be mild, moderate, or serious, depending on how much hemoglobin your body makes. Hemoglobin is a protein that helps red blood cells carry oxygen.

Alpha thalassemia is caused by alpha-globin gene deletion which results in reduced or absent production of alpha-globin chains. Alpha globin gene has 4 alleles and disease severity ranges from mild to severe depending on the number of deletions of the alleles. Four allele deletion is the most severe form in which no alpha globins are produced and the excess gamma chains (present during the fetal period) form tetramers. It is incompatible with life and results in hydrops fetalis. One allele deletion is the mildest form and is mostly clinically silent.

Beta thalassemia results from point mutations in the beta-globin gene. It is divided into three categories based on the zygosity of the beta-gene mutation. A heterozygous mutation (beta-plus thalassemia) results in beta-thalassemia minor in which beta chains are underproduced. It is mild and usually asymptomatic. Beta thalassemia major is caused by a homozygous mutation (beta-zero thalassemia) of the beta-globin gene, resulting in the total absence of beta chains. It manifests clinically as jaundice, growth retardation, hepatosplenomegaly, endocrine abnormalities, and severe anemia requiring life-long blood transfusions. The condition in between these two types is called beta-thalassemia intermedia with mild to moderate clinical symptoms.

Hemoglobin (HbE) is also a common Hb variant found in Southeast Asia population. It has a correlation with a beta-thalassemia phenotype, as people with thalassemia in this territory are commonly found to have HbE.

Two new terminologies being used more often in clinical settings are transfusion requiring and non-transfusion requiring thalassemias and all the basic classification falls into these two types depending on the requirement of frequent blood transfusions or not.[1,2,3]

Etiology

Thalassemia is autosomal recessive, which means both the parents must be affected with or carriers for the disease to transfer it to the next generation. It is caused by mutations or deletions of the Hb genes, resulting in underproduction or absence of alpha or beta chains. There are over 200 mutations identified as the culprits for causing thalassemias. Alpha thalassemia is caused by deletions of alpha-globin genes, and beta thalassemias are caused by a point mutation in splice site and promoter regions of the beta-globin gene on chromosome 11.[4]

Epidemiology

According to Director General Thalassemia Foundation Punjab, Thalassemia is the commonest inherited disorder in Pakistan over 6000 affected children who born annually with Thalassemia Major, meaning 17 affected children born each day in Pakistan. He further added that psychosocial interventions play a vital role in the prevention of genetic disorders.

Alpha thalassemia is prevalent in Asian and African populations while beta-thalassemia is more prevalent in the Mediterranean population, although it is relatively common in Southeast Asia and Africa too. Prevalence in these regions may be as high as 10%. The true numbers of thalassemia affected patients in the United States are unknown, as there is no effective screening method in place.[4]

Symptoms

There are different types of thalassemia. The symptoms that you have depend on the type and how serious it is.

Symptoms of severe thalassemia can include:

- Tiredness, also called fatigue.
- Weakness.

- A change in skin color or a yellowing of skin and eyes.
- Changes or problems with facial bones.
- Slow growth.
- Swelling of the stomach area, also called the abdomen.
- Dark urine.
- Poor appetite.

Some babies show symptoms of thalassemia at birth. Others get symptoms during the first two years of life. But some people with thalassemia don't have symptoms.

Diagnosis

Most children with moderate to severe thalassemia show symptoms within their first two years of life. If your child's health care professional thinks your child might have thalassemia, blood tests can confirm it.

Blood tests can reveal the number of red blood cells and irregular changes in their size, shape or color. Blood tests also can be used to look for gene changes in DNA.

Prenatal testing

Testing can be done before a baby is born to find out if the baby has thalassemia. Testing also can determine how serious the condition might be. Tests used to find thalassemia in unborn babies include:

- **Chorionic villus sampling.** This test involves removing a tiny piece of the placenta. The placenta is the organ that forms during pregnancy to give a baby oxygen and nutrients in the womb. Once removed, the placenta sample is checked by a lab. Most often, it's done around the 11th week of pregnancy.
- **Amniocentesis.** This test involves checking a sample of the fluid that surrounds the unborn baby in the womb. The test usually is done around the 16th week of pregnancy.

Treatment

Mild forms of thalassemia trait don't need treatment.

For moderate to severe thalassemia, treatments might include[5,6]:

- **Frequent blood transfusions.** It's common to need these. Some people need them as often as every few weeks. Over time, blood transfusions cause a buildup of iron in blood. That can damage the heart, liver and other organs.
- **Chelation therapy.** This treatment removes extra iron from the blood. Iron can build up due to regular transfusions. Some people with thalassemia who don't have regular transfusions also can develop excess iron. Removing the excess iron is vital for your health.

To help rid your body of the extra iron, you might need to take medicine by mouth. The medicines include deferasirox (Exjade, Jadenu) or deferiprone (Ferriprox). Another drug called deferoxamine (Desferal) is given through a needle in a vein.

- **Other medicines.** A medicine given by shot called luspatercept (Reblozyl) helps some people need fewer blood transfusions. A medicine taken by mouth called hydroxyurea (Hydrea, Droxia) can lower the chances of getting other health problems because of thalassemia.
- **Stem cell transplant.** This also is called a bone marrow transplant. Sometimes, it might be a treatment option. For children with severe thalassemia, it can get rid of the need for lifelong blood transfusions and drugs to control iron overload.

A stem cell transplant involves receiving infusions of stem cells from a donor with matching cells, often a healthy sibling.

Risk factors

Factors that raise your risk of thalassemia include:

- **Family history of thalassemia.** The condition passes from parents to children through genetic changes in hemoglobin genes.
- **Certain ancestry.** Thalassemia happens most often in people of South Asian, Italian, Greek, Middle Eastern or African descent.

Complications

Health problems that can stem from moderate to severe thalassemia include[7]:

- **Iron overload.** People with thalassemia can get too much iron in their bodies. This can be due to the disease or to frequent blood transfusions. Too much iron can result in damage to the heart, liver, and glands that make and release hormones.
- **Infection.** People with thalassemia have a higher risk of infections. This is especially true if they've had their spleens removed.

Severe thalassemia can lead to the following health problems:

- **Bone changes.** Thalassemia can cause the spongy tissue inside some bones, called bone marrow, to expand. That makes bones widen. It can lead to an irregular bone structure, especially in the face and skull. Expanding bone marrow also makes bones thin and brittle. That raises the chance of broken bones.
- **Enlarged spleen.** The spleen is an organ that helps the body fight infection. It also helps remove old or damaged blood cells. Often, thalassemia happens along with the destruction of a large number of red blood cells. This causes the spleen to get bigger and work harder than usual.

An enlarged spleen can make anemia worse. It also can reduce the life of red blood cells received in a transfusion. If your spleen grows too big, your health care professional might recommend surgery to remove it.[8,9]

- **Slowed growth rates.** Anemia can slow a child's growth and delay puberty.

- **Heart problems.** Congestive heart failure and irregular heart rhythms can be linked with severe thalassemia.

Prevention

Thalassemia is a preventable disease and our hope lies in adopting a preventive program on the line pursued by countries like Italy, Cyprus and Iran, who have resulted in either complete control of significant reduction in the births of new Thalassaemic Major children in these countries.

Awareness among general public with the global community as one to improve thalassemia knowledge, is an open call to action to all supporters to promote awareness about thalassemia and its global impact and share essential information and knowledge to support the best possible health, social and other care of people affected by this disease.

Most of the time, you can't prevent thalassemia. If you have the condition or if you have the thalassemia gene changes that cause it, it is very important to talk with a genetic counselor. The counselor can offer advice on the risks of your children being affected.

Some people with thalassemia major think about getting pregnant with assisted reproductive technology. This includes procedures such as in vitro fertilization. IVF joins an egg and a sperm outside the body to make the earliest stage of an unborn baby, called an embryo. An exam called preimplantation genetic testing can then be used to check the embryo for gene changes related to thalassemia. If an embryo doesn't have these changes, it can be placed in the uterus to start a pregnancy. This might help people who have thalassemia or a related gene have healthy babies.

Another procedure that might lead to pregnancy is called intrauterine insemination. Sperm from a donor who doesn't have thalassemia or the genes related the condition is placed in the uterus to join with an egg.

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