

Indian Academy of Pediatrics (IAP)



GUIDELINES FOR PARENTS

Thalassemia: What Parents Need to Know?

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10 FAQs on THALASSEMIA: WHAT PARENTS NEED TO KNOW?

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Thalassemia: What Parents Need to Know?

Q1

What do we mean by thalassemia?

Thalassemia is a single gene (inherited from parents) blood disorder caused by reduced production of a protein called globin chain which is required in the right amount to form a normal, stable hemoglobin, an important part of red blood cells. These red cells with such hemoglobin cannot function properly, and they last shorter periods of time in the blood circulation, causing anemia due to defective circulating red cells.

Red blood cells carry oxygen to all the cells of the body. Oxygen is required for all the cells of the body, without which they cannot function well. Anemia due to thalassemia causes easy fatigability, feeling of tiredness, weakness, or shortness of breath. Anemia can also affect organs adversely and cause death.

Q2

How is thalassemia classified?

In intrauterine life, the hemoglobin (the protein inside the red cells in the human body) is composed of mainly fetal hemoglobin, which is made up of 2 α (alpha) and 2 γ (gamma) chains, and this constitutes 70% of the hemoglobin at birth. After birth, the fetal hemoglobin slowly transitions into adult hemoglobin (HbA) which constitutes approximately 95% of the total hemoglobin by 6 months of age, and this is composed of 2 α (alpha) and 2 β (beta) chains. These chains are produced through signals by normal genes in the cells of the bone marrow that produce the red cells. For α (alpha) chains, there are a total of four genes responsible, two inherited from each parent. Whereas for β (beta) chains, there are two genes, one each from the mother and the father.

Reduced or absent synthesis of α -globin chains and β -globin chains cause α -thalassemia and β -thalassemia, respectively. In India, our children suffer more commonly from β -thalassemia and, therefore, when we refer to thalassemia in India, we mean β -thalassemia.

Based on the number of genes that are abnormal or defective, thalassemia is termed as “thalassemia minor/carrier/trait” and “thalassemia major” or “thalassemia intermedia”. When one gene is defective and the other gene is normal, we term the state as “thalassemia minor/carrier/trait”. Whereas, when both genes are defective, it is called as “thalassemia homozygous”—which could be *clinically mild (not requiring regular transfusions) and called as thalassemia intermedia, now referred to as nontransfusion dependent thalassemia (NTDT) or clinically severe, i.e., thalassemia major (requiring regular frequent transfusions) now known as “transfusion dependent thalassemia (TDT)”*.

What is Thalassemia Minor/Carrier/Trait?

As mentioned earlier, every person has two genes which control formation of β -chains, which are part of hemoglobin in our body. Thalassemia trait/minor/carrier is a person with one normal gene and one defective gene. Such persons have mildly decreased β -chain production and, therefore, a slightly lower than normal hemoglobin. However, they are like any normal person and do not require any treatment. They are usually unaware about their carrier state, unless they undergo a blood test called “HPLC”. Once you are aware of your thalassemia minor status, please inform your doctor about it and do not take iron supplements unless you have proven iron deficiency anemia by doing some blood tests for estimating the iron in your body.

How do I know that I am a Thalassemia Minor/Carrier/Trait?

A simple blood test called *high performance liquid chromatography (HPLC) or hemoglobin electrophoresis for hemoglobin variants* can detect thalassemia carrier. This is required to be done only once in lifetime.

Everyone should be aware about their thalassemia status before planning to have children to avoid thalassemia major in their child.

What is β -thalassemia Major or Transfusion Dependent Thalassemia?

Beta-thalassemia major is a genetic (or “inherited”) blood disorder that is also called Cooley’s or Mediterranean anemia or sometimes simply called “thalassemia”. β -thalassemia major, the most severe form of the disorder, prevents or greatly reduces the body’s ability to produce “adult” hemoglobin (Hb) and causes severe anemia requiring blood transfusions.

Q3

How did my child get it?

Beta-thalassemia major is an inherited disease. When *both parents are thalassemia carriers or minor or traits*, their child could be born with thalassemia homozygous, i.e., thalassemia major/intermedia or TDT/NTDT. There is a *1-in-4 (25%) chance during each pregnancy that the child will be born with a severe form of the disease, i.e., thalassemia major or intermedia (both defective genes), 2-in-4 (50%) will have thalassemia carrier status (one normal gene and one defective gene) and 1-in-4 (25%) will be unaffected or normal (both normal genes), when both husband and wife are thalassemia carrier or traits or minor (Fig. 1).*

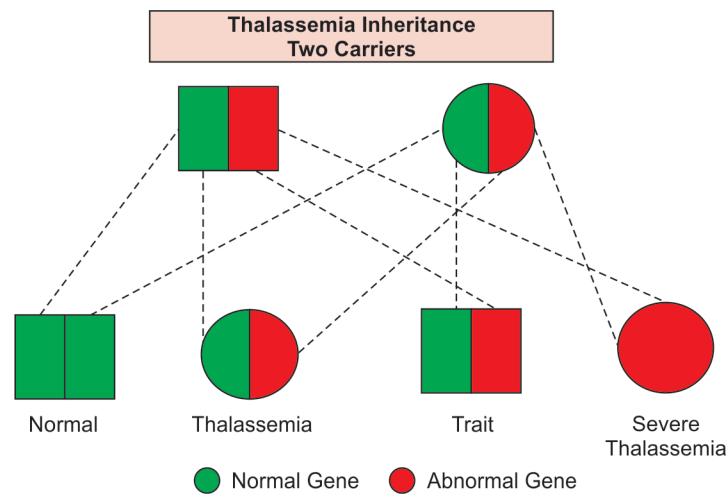


Fig. 1: The chances of having a child with thalassemia in each pregnancy when both parents are carriers.

Is it my fault, if my child is born with thalassemia major (TDT)?

No. Just as you cannot control what color eyes your child will inherit, you cannot control whether your child will inherit thalassemia. However, getting yourself tested for thalassemia carrier/minor/trait status prior to pregnancy enables you to discuss options with the doctor to know what you could do so that you have a normal child.

Q4

What are the signs and symptoms of thalassemia major (TDT)? What should I look for in my child?

Babies who are born with transfusion-dependent thalassemia are perfectly normal till about first 3–6 months of life. After which they start looking pale, are more irritable, do not feed well, do not grow well, and develop enlarged liver and spleen as they grow. Unless diagnosed in time and treated adequately, they may develop hemolytic or chipmunk facies, i.e., prominence of certain facial bones—fronto-parietal prominence, malar prominence, malocclusion of teeth, etc. (**Fig. 2**).



Fig. 2: Hemolytic facies in a child with transfusion-dependent thalassemia.

The most important things to look for include:

- Is your child looking pale?
- Is your child growing well or gaining weight adequately?
- Is your child's appetite decreasing?
- Does his or her belly look bigger?
- Is your child crying a lot or is irritable?
- Does your child feel excessively sleepy/tired?
- Does your child suffer from repeated infections?
- Anything else that is out of the ordinary.

What will Happen to my child now that he has Thalassemia Major or Transfusion-dependent Thalassemia?

Medical treatments have improved greatly over the years; there is reason to believe that your child, taking advantage of the therapies available now and in the future, will live a long and full life.

Q5

What is the treatment of TDT? Is there a cure?

Red Blood Cell Transfusions

Regular red blood cell transfusions (**Fig. 3**) are the lifeline of a child with thalassemia major or TDT. The hemoglobin should be maintained at 9–10.5 gm% before transfusion. They should receive packed red cell transfusions, preferably without white cells (leukodepleted, **Fig. 4**) every 3–4 weeks, and this frequency might increase as the child grows.



Fig. 3: Transfusions in a “daycare center”.

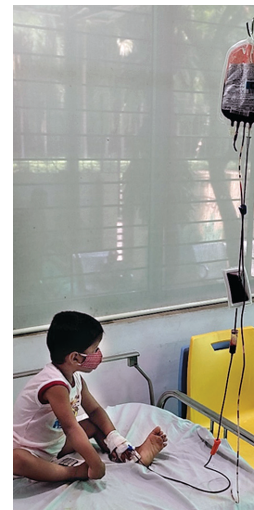


Fig. 4: Bedside leukocyte filter.

Chelation Therapy

Repeated red cell transfusions lead to iron overload in these children. This iron gets deposited in various organs of the body including hormone-producing endocrine glands (such as thyroid gland, parathyroid glands, pituitary gland, and pancreas), heart, bones, liver, and spleen.

Certain medicines called iron chelators are given to remove excess iron from the body. This would reduce the damage that it causes to the organs. However, they need to be taken in the correct doses as well as regularly for good effect. These are injectable and oral. The injectable medicine, deferoxamine, also known as desferrioxamine, is generally reserved for use in those children who cannot tolerate oral medications due to their side effects. The oral medications include deferiprone and deferasirox. Both are effective and should be consumed regularly as per your hematologist’s prescription.

You will be advised to perform certain blood and other tests regularly to look for any adverse events due to these medications. If you are taking deferiprone, report to your doctor if your child develops joint pains or joint swellings. Additionally, a complete blood count, liver, and kidney functions are required at least on monthly basis to monitor the side effects of the oral chelators. With deferasirox and desferrioxamine, an annual ophthalmology evaluation and audiometry also needs to be done.

Curative Treatment

The curative treatment for thalassemia major (TDT) is hematopoietic stem cell transplantation (HSCT) popularly known as “bone marrow transplant (BMT)”. It can be done with a full HLA-matched sibling/family donor or an matched unrelated donor (MUD) for a successful outcome. The treatment center will recommend that your family should be tested to look for a “match” in case you are interested in this option. If there is a matched donor available, you and the treatment center staff will review the options and make decision for transplant or medical treatment. As the best results are obtained in children younger than 8–10 years of age, this option should be considered at an early age of the child.

Q6

What are some of the complications of red blood cell transfusions, and what should I do to prevent or treat them?

The most common complications of transfusions are fever and allergic reactions. Leukocyte filters (**Fig. 4**) help to significantly reduce the non-hemolytic febrile transfusion reactions (fever with chills after transfusions). *Allergic reactions* are due to proteins in the blood plasma and can be managed by certain simple medications which will be prescribed by your treating doctor. If these occur recurrently, triple saline washed red cells can be given.

Report to your doctor immediately, if your child develops fever, breathlessness, palpitations, excessive pain in abdomen, jaundice, skin rashes or dark or red-colored urine, following transfusion. This could suggest a transfusion-related complication.

There is a *risk of viral infections* with transfusions, but the likelihood of transmission is *exceedingly small* because the donated blood is tested for hepatitis B, hepatitis C and HIV, syphilis, and malaria. Nucleic acid amplification

tests (NAAT) tested red cell transfusions can reduce the risk of viral infections further but are presently not a standard of care in the country.

Finally, there will be *iron overload* after a couple of years of transfusions. This requires removal of the iron with medication as mentioned earlier.

To monitor for complications of *iron overload*, follow your doctor's advice. Certain tests need to be done annually to diagnose these complications and treat them. Five years onward, a blood sugar and thyroid profile, 7 years onward, a DEXA (dual emission X-ray absorptiometry) scan and a T2-weighted MRI for iron overload in the heart, liver, pituitary, and pancreas is indicated. At 10 years onward, growth evaluation and hormonal tests as indicated. Starting at the age of 12 years in girls and 14 years in boys, annual evaluation for attainment of puberty and accordingly, related tests might be required.

Q7

Can my child go to regular schools, get regular vaccines, play with other kids, etc.?

Yes, your child is like any other child. With proper treatment, your child will grow like any other child. S/he can get regular vaccines—ensure that hepatitis B as well as hepatitis A vaccines have been administered to your child as these will protect the liver from these viruses. S/he can attend regular school, play with other children, etc. The disease is genetic and does not get transmitted from one to another.

Does my child need any specific diet or nutritional supplements?

Nutrition of your child is particularly important. You are advised to encourage your child to eat a balanced diet consisting of dairy products, grains, fruits, and vegetables. Avoid excessive intake of iron rich foods in diet such as red meats, beans, raisins, dates, jaggery, almonds, and green leafy vegetables. Also avoid cooking in cast iron cookware. Drinking tea or coffee along with meals can be helpful as tannin can impair iron absorption. Supplements including vitamin D, calcium, and zinc (especially for those on deferiprone) are advised.

Q8

Will my child be able to marry and have children?

Yes, your child will be able to marry. If appropriate and regular treatment is taken, people living with thalassemia achieve puberty and can also conceive. Discuss this with your doctor since the age of puberty evaluation. However, the rule of inheritance based on the partner's status for thalassemia would decide the status of the offspring. If your child is undergoing BMT, please discuss the fertility status and outcomes with the treating BMT physician about the same.

BMT cures the disease in the index case, but the thalassemia genes can still be passed on to their progeny. This should be discussed with your doctor.

Can this disease affect our future pregnancies? If so, can it be prevented?

Yes, as mentioned earlier, the chances of having a thalassemia major or TDT child is *25% in each pregnancy*. Genetic studies in the child with TDT as well as the parents are essential for diagnosing the fetus in the next pregnancy. This should be done before planning the next pregnancy. Prenatal diagnosis in the first trimester of pregnancy (between 10 and 15 weeks) by chorionic villus sampling (CVS) can be done to determine the thalassemia status of the fetus and decision to continue or not should be taken in consultation with the treating doctor.

Q9

Are our relatives at risk of getting a child with thalassemia? How can we identify it?

Yes, your relatives are at a higher risk of being thalassemia trait or carriers and having a child with thalassemia major (TDT) as the gene is more common in certain communities. Your extended family, especially children and young persons in reproductive age groups, must be encouraged to undergo testing with HPLC or hemoglobin electrophoresis to know their status. They should undergo counseling, if both partners in a marriage are thalassemia carriers or trait.

Q10

Does the government and the society offer any support to my child due to her/his special needs?

Thalassemia has been certified as a disability by the Government of India in 2016. Your child is eligible for a disability certificate, which can be obtained from a government hospital. This will provide her/him access to inclusive education in government/government-recognized educational institutes, reservation in government jobs, and social welfare schemes such as reservation in allocation of land and poverty alleviation schemes.

Groups like Red Cross Society, Thalassemia International Federation, Thalassemia Welfare Society and *Thalassemia* Patient Advocacy Groups (PAGs), and various other local thalassemia societies formed by parents' groups offer considerable support to children with thalassemia and their families. As parents of a child with thalassemia, it is also your duty to spread awareness about voluntary blood donation among friends, relatives, and colleagues as well as encouraging healthy young volunteers to enrol themselves for bone marrow donor registries too.