What Should One Know About Thalassaemia Minor

What Is Thalassaemia?

- Thalassaemia is a common inherited genetic disorder of hemoglobin (Hb).
- To understand Thalassaemia one should know a bit more about Hb and its Structure & function.

Understanding BLOOD & Its Components?

- The Oxygen from lung is carried to tissues by a molecule called Hemoglobin
- Hemoglobin is packed in Red Cells.
- Besides Red cells (RBC) our Blood also contains White blood cells (WBC) and Platelets.
- The WBCs are our defense cells and they help us fight infections.
- Platelets: are tiny cells that help clot blood along with other coagulation factors.
- The liquid portion of Blood is called plasma.

What Is Hemoglobin?

- Hemoglobin (Hb) is pink red in color & it carries Oxygen from lungs to tissues.
- RBC life is 120 days and our Bone Marrow daily produces > 200 billion RBCs to replace 0.8% of Blood lost daily.
- To understand the nature of defect in thalassaemia one has to understand the structure of HB.

Tell Us About Structure Of Hemoglobin?

- The structure of HB resembles a transport vehicle.
- Heme forms the centre of Hb & is very similar to the chassis of a vehicle;
- The front & back wheels are protein attachments called alpha & Beta chain (See fig 1).
- All components are manufactured by genes at different sites and finally assembled to form complete Hb molecule see fig 1.

How Is Hemoglobin Manufactured In Our Body?

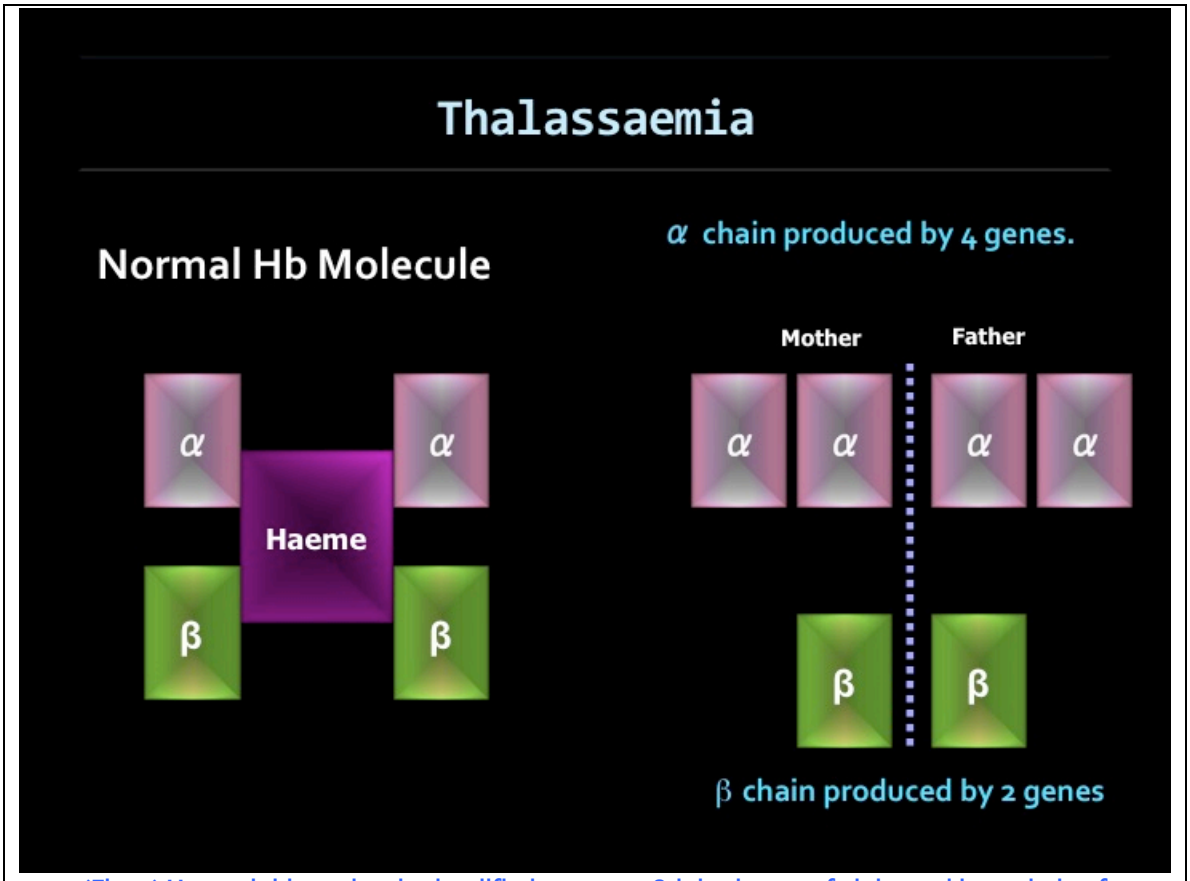
- α chain, β chain and heme are manufactured at different sites in the erythroid cells and finally assembled in to a complete HB molecule.
- For alpha chains we have 4 genes **($\alpha\alpha$ / $\alpha\alpha$)** see fig 1.
- While for beta genes we have 2 genes (β/ β) see fig 1.
- Half of these genes we receive from our mother and half from father as shown in **fig 1.**

What Is The Defect In Thalassaemia?

- Thalassaemia is basically a **quantitative** defect of these chains.
- Those with **an α** chain defects are called **α Thalassaemia.**
- Those with **β** chain defects are called **β Thalassaemia.**

What is the Genetic of Thalassaemia?

- Thalassaemia is a genetic defect acquired at birth.
- One is born with it and will carry this defect through out one's life.
- **You can also pass on this defect to your children**



(Fig. 1) Hemoglobin molecule simplified structure & inheritance of alpha and beta chain of hemoglobin.

What Are The Clinical Types Of Thalassaemia?

- **Clinical types of β Thalassaemia:**
  - **β Thalassaemia Minor:** mild defect in which one out of two β chain gene is defective. i.e. one good gene and one bad gene. **(β /-)** see fig 2.
  - **β Thalassaemia major**: severe defect in which both the β chain gene is defective

    (- / -) Both β genes defective

Children born with Thalassaemia major needs life long blood transfusion to survive.

"Knowledge about thalassaemia is important to prevent the birth of a child with thalassaemia major."

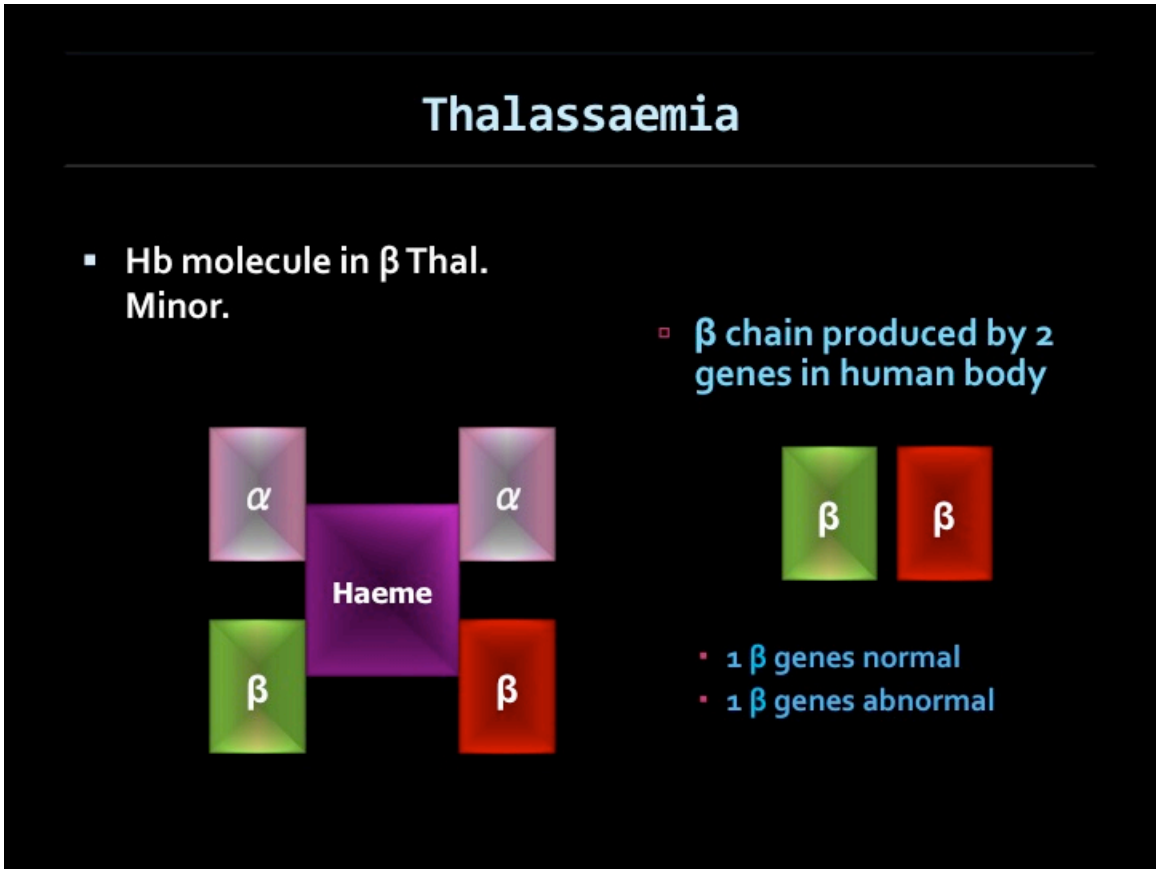


Fig 2: show the defect in β Thalassaemia Minor where there is quantitative defect in one β chain.

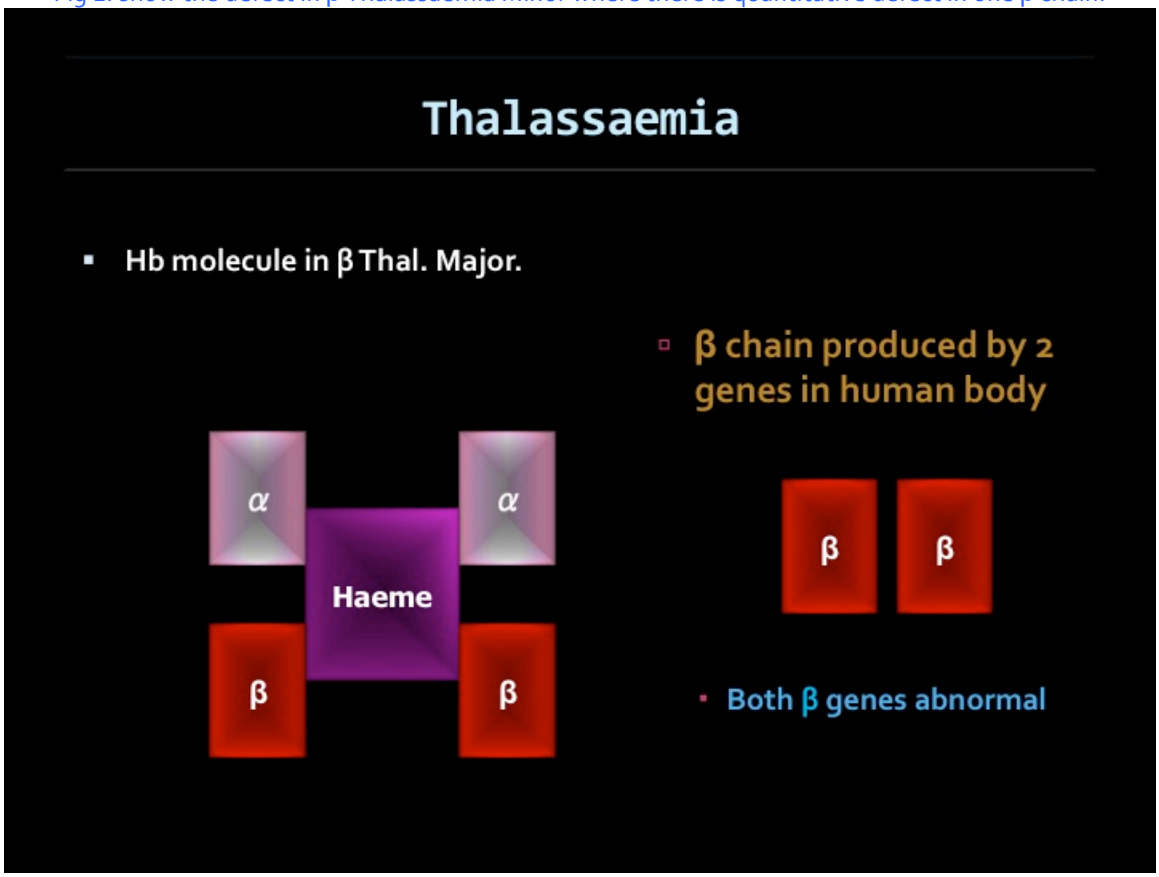


Fig 3: show the defect in β Thalassaemia Major where there is quantitative defect in both β chains.

What Is The Magnitude Of Problem?

- Thalassaemia minor is extremely common in India and the south East Asian countries and the Mediterranean countries.
- There would be more than 30 millions cases of thalassaemia minor or traits in our country.
- Thalassaemia minor is more common among certain communities like Lohanas, Kutcchis, Sindhis, Bhanushalis, Khojas, Jains, Neobuddhists, Bhatias, Punjabis, agarwals, Muslims, Bengalis and various tribal groups though almost anybody could have this genetic defect.
- The prevalence rate of **β Thalassaemia Minor** among certain communities may vary from 1 % to 5 %.
- Every year more than 10,000 children with thalassaemia major are born in our country.

Thalassaemia Minor Or Thalassaemia Carrier How Do We Identify Them?

- **β Thalassaemia Minor** is often asymptomatic.
- **β Thalassaemia Minor** may be recognized when there is a child with thalassaemia major born in the family.
- β Thalassaemia minor may present with mild refractory anemia (HB between 9 to 11 gm/dl)
- Exaggeration of anemia during pregnancy.
- In the CBC report of an individual; if RBC count is > 5.0 million with mild anemia or if MCV/RBC ratio is < 11 it favors β Thalassaemia Minor.

How Does One Diagnose β Thalassaemia Minor?

- Do HB electrophoresis. HbA2 value of > 3.5 confirm β Thalassaemia minor.
- Preferably do Hb Electrophoresis by HPLC for accurate values of HbA2
- In high-risk communities screening for β thalassaemia minor is very rewarding, especially in the marriageable age group.

What Is The Implication Of Diagnosis Of β Thalassaemia Minor For An Individual?

- An individual with β Thalassaemia minor has mild anemia with Hb in range of 9 to 11 gm / dl. Which is often unrecognized
- There is no effect on his life span or his routine activity.
- Anemia may get exaggerated temporarily during pregnancy.
- The most important implication is genetic.

Genetic Counseling:

- **If Both Husband And Wife Are Thalassaemia Minor The Possibilities Are Shown In Fig 4.**
    - **There is 25% of having a child with Thalassaemia Major**
    - **25% chance of child being Normal**
    - **50% chance of child being Thalassaemia Minor**

- **If One Of The Partners Is Thalassaemia Minor And One Of Them Is Normal The Possibilities Are Shown In Fig 5.**
    - 50% chance of child being Normal.
    - 50% chance of Child having β Thalassaemia Minor.

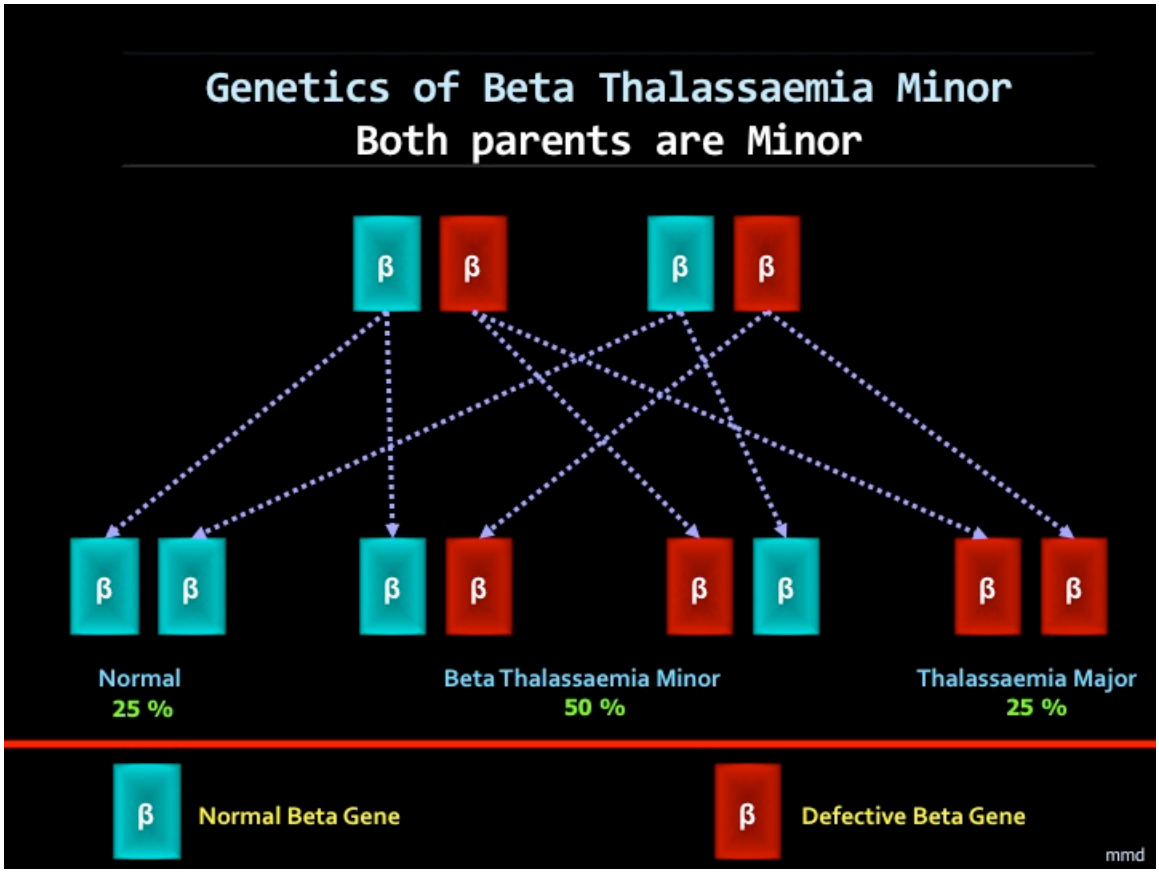


Fig 4: Possibilities when both parents are b Thalassaemia Minor

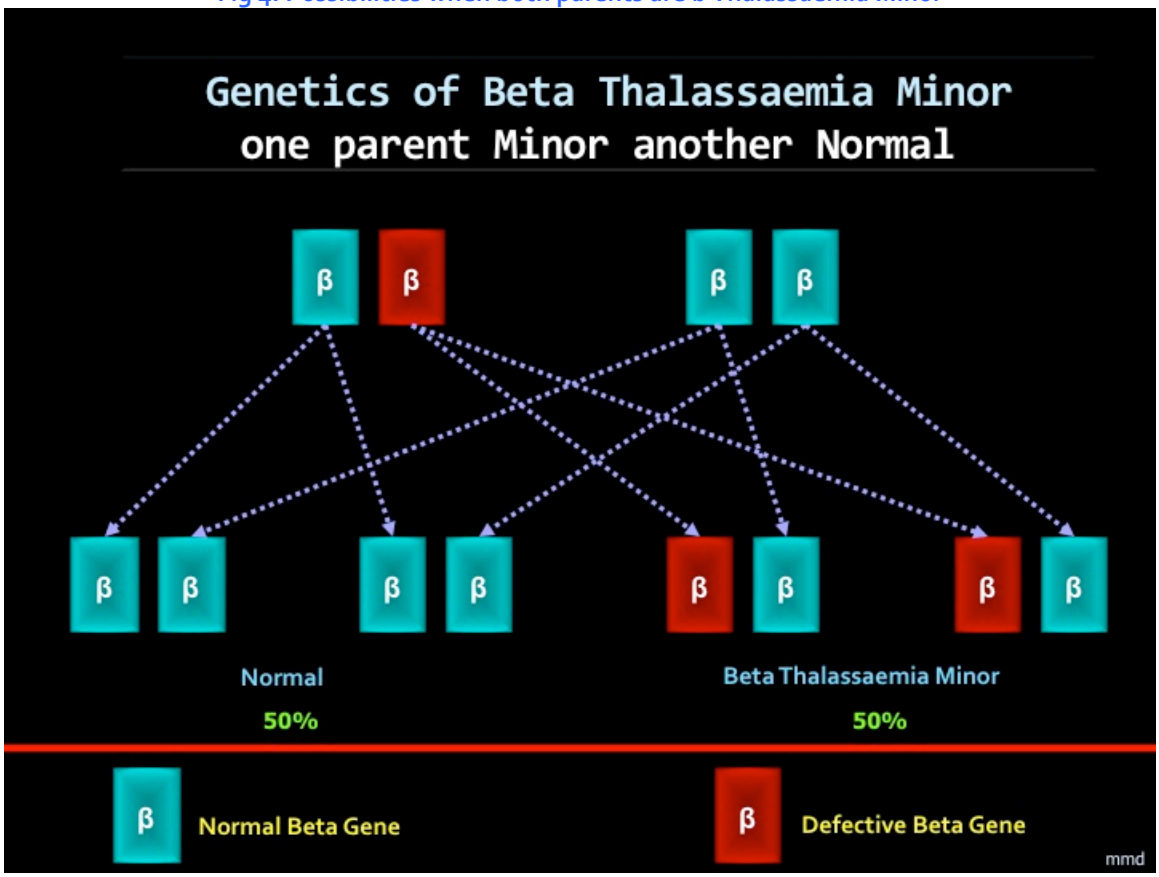


Fig 5: Possibilities when one parent is Normal & other parent is β Thalassaemia Minor

How Can We Prevent The Birth Of Child With Thalassaemia Major?

- If you are from one of the high-risk communities Test your self for thalassaemia minor before marriage.
- If you have thalassaemia minor then test your spouse and other family members for thalassaemia minor.
- If both Husband and wife have thalassaemia minor, for every pregnancy, they should go for antenatal diagnosis to find out whether the child to be born is normal, minor or major. In case the test show the fetus to be thalassaemia major then a decision regarding continuation of pregnancy has to be made.
- These antenatal tests are available in various centers in India
- Details about the antenatal diagnosis can be found at www.thalassaemia.org

Thalassaemia Major:

- Every year there are more than 10,000 children with thalassaemia major born in India.
- India has more than 100,000 cases of thalassaemia major.
- Children born with Thalassaemia major as the name suggests has a major problem with defects in both the ß genes.
- Most are symptomatic by the age of 1 to 2 years with severe anemia, liver and spleen enlargement and bony changes.
- They need life long blood transfusion for their survival.
- Blood transfusion is required once every 3 to 4 weeks to always maintain HB above 9 to 10.5 gm/dl.
- Lifelong blood transfusion has its own problems like Tx reactions, transmission of viral infections like HIV, HbsAG, HCV, other viruses; Iron overload.
- Every unit of transfusion gives the child approximately 200 to 250 mg of elemental iron
- Body do not have any effective means of excreting iron hence iron accumulation occurs in various organs of the body like liver, heart, Testes, pancreas, joints, parathyroid, thyroid, Skin resulting in damage to these organs.
- Death generally is secondary to heart and or liver failure.
- To remove excess iron from the body these children need to take some form of iron chelation with either desferal or Kelfer or Asunra, which also has its own problem.
- Some children the need for blood transfusion increases dramatically due to hyper functioning spleen in which case splenectomy will help the child.
- These children need psychological support from doctor, family and professional help when necessary.
- The median survival of a child with thalassaemia major in our country is approximately 15 to 20 years.
- The survival rate is improving and instances of thalassaemia major children having attained adulthood, married and having their own children are seen more frequently.
- Hope and positive attitude is of great help.

Can We Cure Thalassaemia Major?

- The only curative treatment is Bone Marrow Transplantation (BMT).
- BMT costs approximately 8 to 10 lakhs of rupees and a completely matched sibling donor for BM stem cells.
- There is no risk to the donor
- Alternative source for stem cells is umbilical cord blood.
- The success rate with BMT in completely matched sibling donor is almost 80 %
- The success rate decreases with advanced liver disease in the recipient, if it is a matched but unrelated donor.

Are There Any Research Treatments Available?

- There is tremendous research interest in Gene therapy.
- Since thalassaemia occurs because of a defective gene it is possible to replace this abnormal gene and the child can be cured.
- This is the future treatment and expectations are very high.
- Gene therapy should become available by next decade.

Points To Remember; "Clinical Pearls"

- There are more than 30 million thalassaemia minor carriers in India
- You could be one of them. It is not a taboo
- Do a test for Thalassaemia minor even if you appear to be healthy especially if you belong to high-risk community.
- If you have thalassaemia minor check whether your spouse / spouse to be is a thalassaemia minor.
- If both you and your spouse have thalassaemia minor, do a prenatal test by chorionic villous sampling very early in pregnancy.
- Our aim should be to prevent the birth of child with thalassaemia major
- Spread awareness about thalassaemia.
- Children afflicted with Thalassaemia Major need our compassion and support.
- All Doctors have an obligation to Society to pick up tell tale signs, which suggest presence of **β Thalassaemia Minor** on CBC report, like an RBC count > 5.0 million suggesting ineffective erythropoiesis; & MCV/RBC Ratio < 11 favoring the possibility of β Thalassaemia Minor.

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