THALASSAEMIA -

PREVENTION IS THE BEST OPTION FOR DEVELOPING COUNTRIES - SRI LANKANS CAN CONSIDER "THELASSAEMIA PRONDOMA"

Introduction

To understand thalassaemia, it is important to learn about blood. We have about 5 liters of blood in an adult person (80 ml/kg in a child). Blood has liquid component which is called plasma and cellular component comprising of red cells, white cells and platelets. Red cells are dealing with transport of oxygen from lungs to other organs and carbon dioxide from tissues to lungs. White cells fight infections. Platelets stop bleeding by forming blood clots. Blood circulating all over the body transport nutrients from gut, hormone from endocrine organs, and waste products from all the tissues. Every heart beat pumps about 70 mL of blood and within one minute (beating 75 times) entire blood volume in the body will pass the heart and lung. As 20% of the cardiac output is passing through the kidney, total blood volume will pass the kidney in 5 minutes.

Red blood cells

Thalassaemia is a disorder of red blood cell. There are five million red cells in one milliliter of blood. Red blood cell is a biconcave cell that can change its shape in order to pass through small blood vessels. Hemoglobin gives the redness to red cells. It is the most important constituent within the red cell that will transport oxygen. In one red cell there are 300 millions of these hemoglobin molecules. These hemoglobin molecules have two components; heam and globin. In thalassaemia production of globin is defective. That will lead to premature breakdown and ineffective production of red cells resulting in anemia (lack of redness in blood).

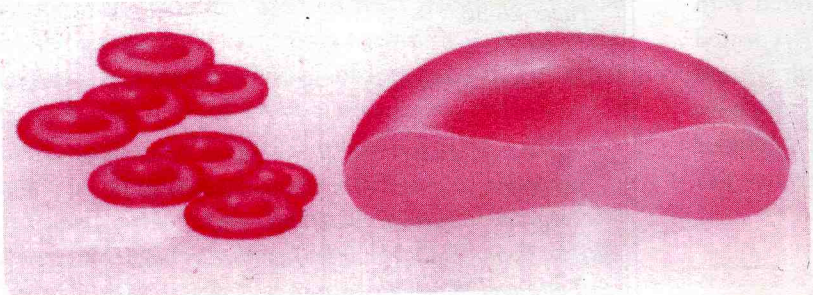

Fig 1 Normal red blood cells (rbc). Enlarged cross sectional view shows the biconcave shape

Genetics and inheritance

Globin is a protein. Synthesis of proteins in our body is controlled by genes. Reason for non production or inadequate production of globin chains is a genetic defect.

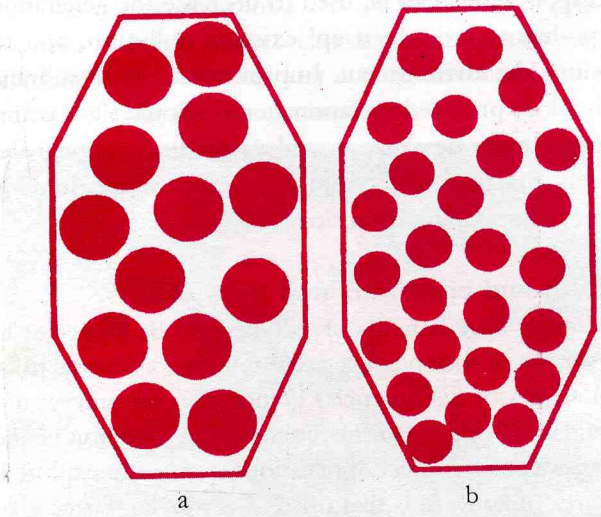

Fig 2 Size difference of red blood cells of (a) an ordinary person, (b) Thalassaemia affected person

Thalassaemia is an inherited disorder of blood leading to premature break down of our red cells causing anemia.

We inherit our genetic material from our parents at conception. These genetic materials are found inside the nucleuses within the chromosomes of almost all the cells in our body. Everybody has 22 pairs of chromosome. In a pair, one chromosome comes from father and the second comes from mother. In addition to this, in males they have one X chromosome (from mother) and Y chromosome (from father). In females they have two X chromosomes one from mother and the other from father.

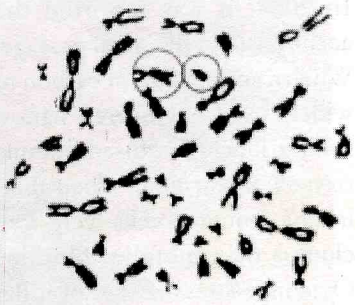

Fig 3 Chromosomes: Chromosomes inside a cell can be visualized by using a technique called karriotype, pictures are taken by electron microscopy. There are 22 paid of chromosomes and X and Y chromosomes in a female

Defective gene is acquired from only one of the parents in some disease conditions. They are called dominant inherited disease. **Disease like thalassaemia, will manifest only if two defective genes were inherited from both parents. This is called a recessive disease. We have a pair of genes to perform one function. We inherit them one each from mother and father. One of them being defective will not produce any symptom. Those who are carrying only one defective gene are called carriers. Even though carriers are not symptomatic, they have a risk of having an offspring with a disease like thalassaemia if they happen to marry another carrier.**

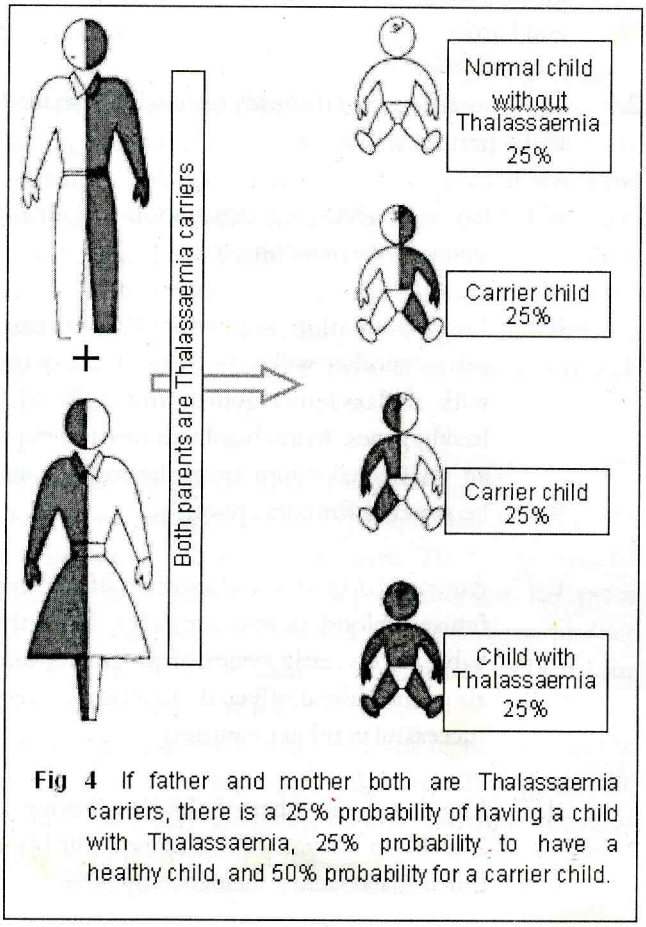

Fig 4 If father and mother both are Thalassaemia carriers, there is a 25% probability of having a child with Thalassaemia, 25% probability to have a healthy child, and 50% probability for a carrier child.

Figure 4 shows how a marriage between two thalassaemia carriers produces a child with thalassaemia. If two thalassaemia carriers (represented as half shaded figures) marry, they have a 25% risk of having a baby with thalassaemia. 50% of their babies will be thalassaemia carriers like their parents. There is only a 25% chance of having a non-carrier normal baby.

How do we prevent having a Thalassaemia Child? The only way for a thalassaemia carrier is to marry a non-carrier. Then none of the children will be affected (Fig. 5). Therefore, marriage between a thalassaemia carrier and a non carrier is the safest approach to prevent birth of a thalassaemia child.

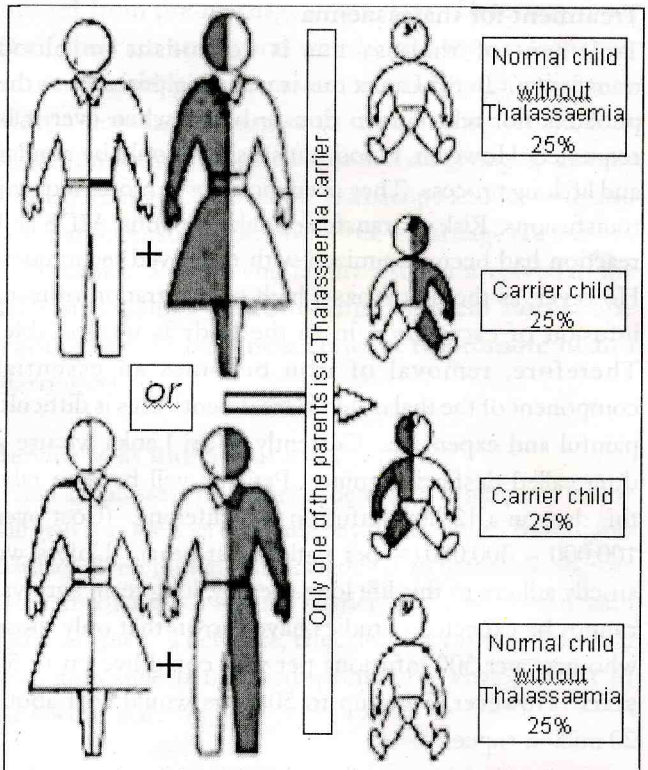

Fig 5 Either father or mother is a Thalassaemia carrier; there is a 50% probability of having a child without Thalassaemia, and 50% probability for a child to be a carrier.

Thalassaemia effects

When a thalassaemic baby is born to a couple who are both carriers, red cells in the baby's blood will get dissolved prematurely and red cell production will be defective leading to anemia; inadequate hemoglobin and red cells. This will affect all the functions of the body including the growth. Child will be pale and lethargic. He will have shortness of breath. Attempt at producing more red cells by expansion of bone marrow will lead to deformities and fractures of bones. Production of red cells in the liver and spleen will lead to massive enlargement of both organs.

At the same time in response to anemia, the gut of the baby will start absorbing more iron even though the child does not having iron deficiency. There is no natural system of iron removal from the body. Iron in excess is toxic and will lead to damage the heart, liver and pancreas leading to heart failure, cirrhosis and diabetes.

Treatment for thalassaemia

Treatment of thalassaemia is dependant on blood transfusion. In Sri Lanka this is not a big problem as the public is not reluctant to donate blood when ever it is requested. However, blood transfusion should be regular and lifelong process. They need monthly or more frequent transfusions. Risk of transfusions like hepatitis, AIDS and reaction had been minimized with improved techniques. However, as the blood has a high concentration of iron, infusion of excess iron in to the body is unavoidable. Therefore, removal of iron becomes an essential component of the thalassaemia treatment. This is difficult, painful and expensive. Currently in Sri Lanka we use a drug called desferrioxamine. Patients will have to take this drug in a 12 hour infusion daily lifelong. (Cost over 100,000 – 300,000/= per patient per year). Unless we strictly adhere to this life long therapy, long term survival cannot be expected. Studies have shown that only those who get over 300 infusions per year could live up to 50 years. However, living up to 50 years would cost about 20 million rupees.

At present the Ministry of Health spends 5% of the health budget on this one single disease affecting 1500 patients. The cost of management is expected to go up in future due to unavoidable cost escalation as we are prolonging the life of patient with an incurable disease leading to accumulation of patients. Many countries, developing and developed, all over the world are using another drug called deferiprone, which is cheaper and considered more effective when used in combination with desferrioxamine. Unfortunately, use of this less expensive drug has been given up by our medical practitioners prematurely due to few case reports of side effects without further evaluation.

Thalassaemia prevention

As this genetic disease is incurable and the cost of management unaffordable, prevention is the only option of managing thalassaemia in Sri Lanka. Thalassaemia prevention should be considered as a way of looking after thalassaemia carriers rather than a programme to eliminate the burden of thalassaemia from a society. This approach will eliminate the feeling of discrimination and ill treatment by medical authorities towards thalassaemia carriers.

Thalassaemia carriers have a problem of running a risk of marrying another carrier and producing a child with thalassaemia. This problem is hidden until their carrier status is checked. **This can be done by a simple blood test called red cell indices for carriers.** This test will measure the volume of red cell (called MCV). Normally it is above 80. Patients with thalassaemia or iron deficiency MCV is below 80. **Both conditions need evaluation and treatment. Accuracy of this test is about 95%.** Scientists are presently evaluating more precise and cost effective tests.

Options available for thalassaemia carriers:

1. Teenage screening and promotion of safe marriages – This is the best option for Sri Lanka. Options that could be adopted when some body is checked after marriage or selecting partner are much difficult and harder.

2. Checking the partner if already selected and decided. If the partner also a carrier;

    a. Consider giving up registration and finally leading to separation

    b. Pre-implantation diagnosis (Thalassaemia carrier mother will have 50% of the ovum with thalassaemia genes, and 50% with healthy genes. In this highly advance technique an unaffected ovum from the mother will be selected for conception)

    c. Antenatal diagnosis and abortion of affected fetuses (blood sample are taken from the baby at very early stages of pregnancy and abort the baby if affected. Considered very successful in other countries)

    d. Limiting the number of children (having 1-2 children instead of 4 children will bring down thalassaemia incidence by 50%)

    e. Take the challenge of looking after a baby with thalassaemia

        1. Bone marrow transplant – Will achieve total cure. Cost only 3 million Rupees. Carried out in India.

        2. Blood transfusion and long term chelation – Life long therapy. Cost 20 million Rupees to live up to 50 years.

Thalassaemia prevention in Iran

Thalassaemia prevention strategy in Iran has set an example for all the developing countries. They implement the project with the basic knowledge of genetics, avoid marriages between carriers. They have tested all the couples when they come for registration of their marriage. Man is tested first. If he is not a carrier, marriage will take place without further testing of women as there is no problem even if she is a thalassaemia carrier.

However, if the man is a carrier then the women is also tested. If she is not a carrier again the marriage takes place with no further testing. If both are carriers, then they are counseled. They will be explained the gravity of the problem and they are allowed to make a decision about their marriage.

Fifty percent of the couples have decided to avoid the marriage and others have restricted their family size. Incidence of thalassaemia in Iran has come down form 1200 before intervention, to 72 cases in 2002. However, as authorities have found significant number of carriers are proceeding with their marriage, abortions have been legalized since 2001. Difficulty in changing the decision when it is offered as late as time of registration is well understood.

Thalassaemia prevention in Cyprus

Thalassaemia prevention in Cyprus started in 1972. At present they don't have new cases. They have offered screening, pre-marriage counseling and abortion. In Cyprus every body is tested and given a card to indicate his/her carrier status; A green card for non-carrier, red card for carrier and violet card for undetermined person. If two persons carrying a red card come for registration of the marriage they are referred to a doctor to explain the problem and they are given options to make decisions about their marriage and family.

Teenage screening for safe marriage

Concept of teenage screening for safe marriage would be the best for Sri Lanka. Considering the experiences in Iran and Cyprus, my suggestion for Sri Lanka is to offer screening and counseling before the young people select their partners. This the basic principal of ***"Uva Thalassaemia Prevention Project"*** *proposed by me in year 2002. Iran has achieved most of its results while abortions were not legalized.*

Pre-marriage counseling is a step forward from antenatal diagnosis and abortion. Teenage screening is another step forward from pre-marriage counseling. Detecting them when they are teenagers, well before they select their partners would leave them with another option; that is to select a non carrier partner to marry. This would be a better and socially accepted option than giving up already decided marriages. Checking horoscope and looking into case and other social factors before a marriage is a custom in Sri Lanka. Parents and family also get involved in the decision making. **Introducing 'medical horoscope reading' would be a new concept to promote health marriages!**

Benefit is at individual level

When a thalassaemia carrier is detected, benefits he or she will gain is as great as detecting any other serious but curable disease. Even though thalassaemia is an incurable disease, problem of a thalassaemia carrier could be solved with 100% efficacy. Therefore, checking for carrier status will have individual benefit irrespective of what the rest of the society is doing.

Attitude of the medical practioners should be just like detecting any other major health problem with appropriate intervention. Revealing the carrier status to a person well before they select their partner would be a great help to an individual and his family,. Therefore, medical doctors should take microcytosis as an important finding and evaluate it properly to conclude whether it is iron deficiency or thalassaemia trait. For this there is no need to have an on going thalassaemia prevention programme in a country.

Is it essential to detect all the carriers?

For a successful prevention programme, detection of all the carriers will be ideal. However, Iran thalassaemia programme has screened only the males and proceed to check female partner only if the male is a carrier. Majority of thalassaemia carrier females would have undergone the marriage without even knowing it. This would be a great relief for females in the Iranian society. This definitely brings down the cost of screening by significant amount.

In Sri Lanka, if we promote to make sure one of the partners (irrespectively of male or female) of a couple to be a non carrier the concept will be more flexible, where even a male carrier also can under go marriage with out been tested.

Safe marriage

When we consider thalassaemia or any other recessively inherited conditions, of one of the partners in a couple is

not a carrier the couple will be safe as far as ihherited condition is considred. When oever we talk about screening programmes, traditionally we talk about detecting all the carriers,. However, as thalassaemia is not a contagious disease, missing carries are not going to spread the disease, Therefore, promoting safe marriages would be more practical and easy option.

If we promote and try to achieve safe marriages rather than detecting all the carriers, majority of the carriers (95% in a society with 5% carriers) will marry somebody who is not a carrier by chance. This will be of great help to thalassaemia carriers as majority of them will not face a problem in finding a partner. Challenge for authorities when launching a thalassaemia prevention programme would be to establish correct attitudes of the society towards marrying a thalassaemia carrier.

Individual responsibility

People living in a thalassaemia prevalent society has an individual responsibility to get them selves checked for their carrier status. While the government should provide much required facilities and support, everybody should screen themselves as it will be for their own benefit. Therefore, such a programme will be sustainable if we have a correct education and approach towards this problem. Even very poor people of Sri Lanka spend large sum of money to arrange their weddings. Therefore, some of this money could be converted for a very useful testing for their own benefit.

Responsibility of medical practitioners

Any medical doctor practicing in thalassaemia prevalent society has the responsibility and duty to evaluate and reveal the thalassaemia carrier status of his/her patients and advice them about the options available depending on the available resources of that country. The routine MCV, MCH should be done once in a life time on all the teenagers just like checking blood pressure or blood sugar in adults. If complied advice given to a thalassaemia carrier will be 100% effective in prevention of having children with thalassaemia.

Responsibility of health authorities and rights of thalassaemia carriers

Our population has 2-4% thalassaemia carriers. Majority of them are distributed in thalassaemia prevalent provinces, North Central, Wayamba and Uva. Their problem is hidden unless they are tested. As the condition is affecting such a large number of people (nearly one million persons) it is the duty of the Ministry of Health to look in to this problem. The carriers have the right to know their problem and solutions available for it.

Following health care policies are proposed for our country;

1. All the people should be given facilities to test their blood for thalassaemia carrier status (at least in Thalassaemia prevalent provinces).
2. For registration of a marriage at least one of the partners should be non carrier person. "having a green card" or
3. The couple should undergo a session of counseling before proceeding with a high risk marriage. High risk marriage is defined as;
   - i. A marriage between two persons who were not screened,
   - ii. Between two thalassaemia carriers
   - iii. Between one unscreened and one thalassaemia carrier.

Only two out of 1000 marriages are expected to be high risk marriages. Therefore, a policy of this nature should not cause any problems in the society.

Responsibility of parents, marriage brokers and horoscope readers

At present 20% of the proposals are given up due to the mismatching horoscopes. Considering thalassaemia carrier status and avoiding a marriage between two thalassaemia carriers has a very strong scientific basis. **Giving up a proposal between two thalassaemia carriers is a very wise decision to avoid a life time agony to a child and a family. Therefore, matching the THALASSAEMIA PORONDAMA would be an essential component to other factors that we consider in selecting partners. However, the final responsibility lies with the man and woman those two who are going to marry and produce healthy children.**

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