INTRODUCTION:

History: The word ‘thalassaemia’ is a Greek term from thalassa, which means "the sea", and emia, which means "related to blood". It relates mainly with Patients discovered in all the Mediterranean countries.

In 1925 two American pediatricians Cooley and Lee described a disease, named Cooley's anaemia, in children of Italian and Greek immigrants, today known as thalassemia major or Mediterranean anaemia.

Background: Though there is no well precise validated data available about the prevalence of thalassemia and related hemoglobin disorders in Bangladesh, it’s presumed from multiple studies that around 3% and 4% of Bangladeshi population are carrier of β thalassemia trait and Hb E trait respectively. As inheritance of thalassemia follow Mendelian pattern, having those fractions of carrier in community, following random marriage, mathematically calculated that roughly 33/10,000 baby born would have β/β thalassemia or Hb E/β thalassemia, which are main types of thalassemia in Bangladesh. There are few other hemoglobin disorders like Hb E diseases have been reported formally or informally which are clinically and hematologically may be dissimilar to β thalassemia. Most of the β thalassemia major and a large fraction of Hb E/β thalassemia patient would die within 1st few decades of life without regular blood transfusion, iron chelation and other supportive treatment. So, transfusion and other modalities of treatment are needed for their normal growth and development. Considering those facts thalassemia is a major paediatric health problem of Bangladesh to be addressed properly to ensure adequate treatment of patients and minimize the birth of thalassemic child by preventive measures to the extent of public concern.

Rational: The inherited haemoglobin disorders are the commonest diseases attributable to single defective genes. They fall into two main groups: the structural haemoglobin variants; Sickle Cell Disease (SCD) and the Thalassaemias which are caused by defective globin production. Carrier numbers of >270 million and more than three hundred thousand children born each year with one of the thalassaemia syndromes or one of the structural haemoglobin variants have been estimated (WHO 1989, 1994). The extremely high frequency of the Thalassaemia disorders compared with other monogenic diseases reflects natural selection and widespread practice of consanguineous marriage. For these reasons the thalassaemias are
most frequent in Bangladesh. These facts have challenged health professionals and policymakers of the country in providing equitable access to quality services for the prevention and treatment of Thalassaemia. The epidemiological data available mainly in Bangladesh underestimate the future health burden resulting from inherited Thalassaemia disorders. For effective addressing the control of these disorders in Bangladesh require considerable work, financial backing and certainly political commitment. Programmes to reduce the number of seriously affected individuals the approaches like:

1. Population screening and counseling programs established to aware people about the risks of having affected children;

2. Population screening or screening in prenatal clinics where if a woman is carrier the partner is screened and if positive, following counseling they are offered a prenatal diagnosis and option to termination of affected fetuses.

Successful prenatal diagnosis programs established in the Mediterranean region resulting in a major reduction in newborns with severe forms of thalassaemias are now available in several other countries such as China, India, Iran, Lebanon, Pakistan, Singapore and Thailand. Whatever are the results of the screening programs they require a proper education of the population about the nature of inherited Thalassaemia disorders. Beside prevention, a main objective is to offer optimum care about management. Ensuring healthy life and promoting wellbeing for all at all ages is essential to sustainable development. Significant strides have been made in increasing life expectancy and reducing some of common killers associated with child and maternal mortality. However, many more efforts are needed to be addressed many different persistent and emerging health issues. For this reason there is an urgent need to bridge a wide gap until every patient in Bangladesh has equal access to quality medical care. An essential means of doing so is through global collaboration on Thalassaemia disorders, enabling all countries to benefit from each other’s experience. The instruments required to support such policies include:

- Epidemiological information and surveillance.
- National guidelines for the diagnosis and management of thalassaemia
- Educational program for health professionals, patients, parents.

The need for management guidelines for Thalassaemias is clear; ensuring access to such guidelines, careful application and implementation should help arriving at early diagnosis, to allow prompt and effective management, early prediction of risk to ensure preventive measures to save unnecessary health care costs.

**Definition:** Thalassaemia is an inherited disorder of haemoglobin characterized by reduced rate of production of globin chain of haemoglobin. It is caused by defect in the gene controlling the production of globin chain of haemoglobin. It is manifested mainly by the features of anaemia resulting from premature destruction of red blood cells.
Patients may have additional clinical features due to complications resulting from increased production of red cells and/or damage to various organs due to increased iron deposition.

PATHOPHYSIOLOGY:

The basic pathophysiological mechanism of thalassemia is imbalance between α group of globin such as α and ζ (zeta) globin and β group of globin such as ε, γ, δ and β globin chains.

Formation of normal stable hemoglobin molecules requires 2 pair of globin chains. One pair of α globin with one pair of β globin chains produce Hb A which is the main fraction of hemoglobin in adult. Same way one pair of α with one pair of δ globin chains produce Hb A2 and one pair of α with one pair of γ globin chains produce Hb F or fetal hemoglobin. Hb A2 normally and consistently present in small amount (2.2 to 3.3%) in normal adult. Hb F is the majority hemoglobin in fetus and decline to <0.5% in adult life. In thalassemia a particular globin chain is reduced such as reduced β globin chain in β thalassemia causing imbalance between α and β globin chains. Excess unbound α globin, due to lack of β globin, remain as free α globin chains which precipitate in red cell membrane making red cell vulnerable to oxidative damage. Similar consequence follows in all non-α thalassemia. However, just opposite thing, the precipitation of β globin chains happens in α thalassemia. This pathophysiological mechanism leads to both extramedullary (hemolysis) and intramedullary (ineffective erythropoiesis inside bone marrow) destruction of red blood cells and their precursors. Ineffective erythropoiesis and hemolysis are responsible for clinical features of thalassemia e.g. anemia, splenomegally, bone deformity etc.
TYPES OF THALASSEMIA:

Genotypic classification:

<table>
<thead>
<tr>
<th>NO. OF GENES PRESENT</th>
<th>GENOTYPE</th>
<th>CLINICAL CLASSIFICATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 genes</td>
<td>αα/αα</td>
<td>Normal</td>
</tr>
<tr>
<td>3 genes</td>
<td>αα/-α</td>
<td>Silent carrier</td>
</tr>
<tr>
<td>2 genes</td>
<td>-α/-α or αα/-α</td>
<td>α thalassemia trait</td>
</tr>
<tr>
<td>1 gene</td>
<td>-α/-</td>
<td>Hb H Ds</td>
</tr>
<tr>
<td>0 genes</td>
<td>-/-</td>
<td>Hb Barts / Hydrops fetalis</td>
</tr>
</tbody>
</table>

CLASSIFICATION OF β THALASSEMIA

<table>
<thead>
<tr>
<th>CLASSIFICATION</th>
<th>GENOTYPE</th>
<th>CLINICAL SEVERITY</th>
</tr>
</thead>
<tbody>
<tr>
<td>β thal minor/trait</td>
<td>β/β+, β/β0</td>
<td>Silent</td>
</tr>
<tr>
<td>β thal intermedia</td>
<td>β+/β+, β+/β0</td>
<td>Moderate</td>
</tr>
<tr>
<td>β thal major</td>
<td>β0/β0</td>
<td>Severe</td>
</tr>
</tbody>
</table>

Phenotypic classification:

- Thalassemia major, e.g. β thalassemia major, severe Hb E/β thalassemia, Hb Bart’s etc.
- Thalassemia intermedia, e.g. β thalassemia intermedia, milder forms of Hb E/β thalassemia, Hb H disease etc.
- Thalassemia minor, e.g. β thalassemia trait, α thalassemia trait, δβthalassemia trait, Hb Lepore etc

Practical phenotypic classification for the purpose of treatment especially transfusion: Best can be expressed by flow diagram given bellow.
CLINICAL FEATURES & DIAGNOSIS:

Clinical feature:

Features of thalassemia major
- Usually present within 2 years of age.
- Failure to thrive
- Repeated infection
- Pallor
- Splenomegaly (and hepatomegaly if not transfused sufficiently)
- May have clinically evidenced jaundice
- Regular transfusion required before 2 year of age for normal growth and development
- Bony expansion causing frontal bossing, malar prominence etc along with growth retardation revealed in childhood if not transfused sufficiently.

Features of thalassemia intermedia
- Very diverse spectrum of expression, severity may ranges from minor to major.
- Usually transfusion independent.
- Mild to moderate pallor after 4 to 6 years of life.
- Pallor, splenomegaly etc become clinically evident after 2 year of age
- Some patient presented with complications of iron over load.
- Some patient may present with features of extramedullary hemopoiesis
- Growth retardation, bone deformity, hepatomegaly only seen in more severe form of poorly treated or untreated thalassemia intermedia.

Diagnosis of thalassemia:

Clinical suspicion on the basis of clinical features
- Pallor/anemia
- Splenomegaly
- Failure to thrive and/or recurrent infection (in <2 year children)
- ± Variable degree of bony change (frontal bossing ± malar prominence ± depressed nasal bridge) and/or growth retardation (in cases of untreated or poorly treated older children and adolescent

CBC:
Hb <9.5 g/dl (9.5 to 11 g/dl with high degree of suspicion from clinical feature and PBF to be referred to expert/hematologist)
- MCV < 75 fl
- MCH < 27 pg
**Peripheral blood film:**
- Marked anisopoikilocytosis (variation in shape and size) (Photomicrograph)
- Target cells
- Nucleated RBCs

**NESTROFT** (Naked Eye Single Tube Red Cell Osmotic Fragility Test) - This test is simple, cheap, easy to perform and effective in detecting Beta thalassaemia trait.

<table>
<thead>
<tr>
<th><strong>NESTROFT Test</strong></th>
<th>Positive</th>
<th>Negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>NESTROFT Test</td>
<td><strong>No Haemolysis of RBC</strong>&lt;br&gt;Therefore, line is not clearly seen</td>
<td><strong>Haemolysis of RBC occurs</strong>&lt;br&gt;Therefore, line is clearly seen</td>
</tr>
<tr>
<td><strong>Decreased Osmotic fragility test</strong></td>
<td><strong>Normal Osmotic fragility test</strong></td>
<td></td>
</tr>
</tbody>
</table>

**Suspected β (Beta) Thalassaemia-a trait**<br>Confirmed by Hb electro/ HPLC<br><br>**Normal person**
A positive test indicates decreased osmotic fragility test.

Capillary hemoglobin electrophoresis (to be able to differentiate Hb E from Hb A2): With clinical feature, CBC and PBF, phenotypic diagnosis of symptomatic thalassemia is likely to be certain. Electrophoresis will identify the genotype of the thalassemia and further confirm the diagnosis.
MANAGEMENT:

Management includes:

❖ Blood Transfusion
❖ Iron Chelation
❖ Pharmacological agents for induction of Hb F
❖ Splenectomy
❖ Bone marrow transplantation
❖ Treatment of Complications
❖ Psychological support

Before going to initiate blood transfusion patients should be categorized as; whether:

- Transfusion dependent
- Non-transfusion dependent

Non-transfusion dependent patients (NTDT):

- Beta Thalassemia intermedia
- Mild /moderate hemoglobin E-beta Thalassemia
- Alpha Thalassemia intermedia(Hemoglobin H disease)
- Hemoglobin E disease
- Beta Thalassemia trait
- Hemoglobin E trait.
- Alpha Thalassemia carrier

These patients can survive and maintain their normal life & daily activities at the hemoglobin level of 6-7 gram/dl.

Occasional blood transfusion needed during stress, infection, surgery, pregnancy, on growth failure, skeletal deformity & huge organomegaly.

So, following parameters of these patients should be followed up:

- Hemoglobin level
- Anthropometry
- Increasing skeletal deformity & organomegaly
- Development of complications like leg ulcer, coagulopathy, pulmonary hypertension & evidences of EMH e.g, cord compression.

Also, to be monitored:

- Serum Ferritin 3 monthly
- T2 MRI yearly (after age of 10 years)
- Endocrine function tests.
Treatment:

➢ Folic Acid & Vitamin supplementation
➢ Fetal hemoglobin inducer like Hydroxyurea, 5-Azacytadine, Thaladomide
➢ Iron chelation (S. Ferritin >800 ng/ml or LIC >5 mg/gram dry weight of liver or >10 years) preferably by Deferasirox. Deferipon or Desferrioxamine can also be given.

Management of transfusion dependent Thalassemia:

❖ Blood Transfusion:

Indications- Hemoglobin level < 8.0 gm/dl.

Before initiation of regular blood transfusion extended blood grouping genotyping to be done.

Product-

- Packed red cell preferably leuco-depleted RBC through Leuco-Filter.
- Washed red cell in case of NHTTR.
- Genotype matched washed red cell in case of Allo-immunization

Volume to be transfused:

- 15-20 ml/kg/day over 3 hours.
- In case of impending HF & severe anemia (Hb<5 gm/dl)-
  5-10 ml/kg/day slowly under coverage of Frusemide.

❖ Iron Chelation:

Indication-

- S. Ferritin > 1000 ng/ml
- After 10-20 Blood Transfusion
- LIC >5 -7 mg/gm dry weight of liver

➢ Inj. Desferrioxamine- 40-50 mg/kg/day S/c infusion over 8-10 hours 5-6 days/week
  Vitamin C 250 mg to be taken orally at the start of infusion.

➢ Deferipon- 75 mg/kg/day orally in 2-3 divided doses. (after 6 years of age)

CBC should be done before & later on monthly to monitor cytopenia, if any then temporarily stop the drug.
Deferasirox-30-40 mg/kg/day orally dissolving in plane water/orange juice 30 minutes before BF.

SGPT & serum creatinine should be done before & later on monthly.

*ICA should be continued by monitoring S. Ferritin level 3 monthly.

Pharmacological agents (Hemoglobin F Inducers):

Hydroxyurea- 10 -20 mg/kg/day orally with 3-4 mg/kg/day increment monthly up to 20 mg/kg/day by monitoring CBC monthly

5-Azacytedine & Thaladomide can also be given.

Complications and Management of complications:

Complications of thalassemia major and their treatment:

The life of patients with thalassemia has improved both in duration and in quality in industrialized countries. Complications are still common and include heart disease (heart failure and arrhythmias), chronic liver diseases, which can evolve in cirrhosis and, rarely, in hepatocellular carcinoma, endocrine problems (hypogonadism, hypothyroidism, diabetes, hypoparathyroidism), stunted growth, osteoporosis, thrombophilia and pseudoxanthoma elasticum.

Complications

Heart

Cardiac problems are frequent during the patients’ life, and heart failure and arrhythmias are responsible for over 70% of all deaths.

Management

Continuous treatment with deferasirox for 2 years at a high dose has been shown to remove iron from the heart in patients with mild, moderate and severe cardiac siderosis.

In patients with severe myocardial siderosis and impaired left ventricular function, combined chelation therapy with subcutaneous DFO and oral deferiprone is indicated.

Liver

Liver disease is frequent in patients with thalassemia, both because the organ is a major site of iron deposition and because of the high prevalence of blood-transmitted infections with hepatotropic viruses. Overall, 0.3–5.7% of thalassemia patients are hepatitis B surface antigen-positive. The prevalence of chronic hepatitis B virus (HBV) infection is higher in Asia and Southeast Asia, whereas HCV chronic infection is common in all countries of the world*.

Liver iron overload is a cause of fibrosis and cirrhosis, especially when associated with HCV infection.
Cirrhosis is a risk factor for the development of hepatocellular carcinoma (HCC) and is a major cause of liver failure.

Management

- The standard of care for the treatment of chronic HCV infection and compensated cirrhosis is the combination of pegylated interferon and ribavirin.
- Pegylated interferon or nucleoside/nucleotide (NUCs) drugs is indicated in hepatitis B ‘e’ antigen (HBeAg)-positive.

Endocrine complications

Iron overload secondary to chronic blood transfusion is the main cause of endocrine complications. Iron deposition and structural damage to the pancreas, the pituitary, parathyroid, thyroid and adrenal glands and to the gonads have been demonstrated histologically.

Hypogonadism

Hypogonadism is the most frequent endocrine complication in patients with thalassemia major. The clinical picture of hypogonadism ranges from total absence of sexual development to arrested puberty, with pubertal development generally at Tanner stage 3, primary amenorrhea in females and testicular volume of less than 6–8 ml in males.

The prevalence of post-pubertal hypogonadism is lower in males than in females.

Management

- In patients with pubertal hypogonadism, early hormone replacement therapy is recommended.

Hypothyroidism

Hypothyroidism is the second most common endocrine disorder.

Management

- Early stages of abnormal thyroid function can be reversed to normal by means of intensive chelation therapy with DFO alone or in combination with deferiprone.
- In patients with subclinical hypothyroidism, therapy should be given for TSH levels greater than 10 U/ml or when symptoms are present.
- In overt primary hypothyroidism, replacement treatment should be given with increasing doses of l-thyroxine.
Hypoparathyroidism
Hypoparathyroidism has been reported to affect 3–20% of patients.

Management
Oral vitamin D and a daily calcium supplement should be given.

Diabetes: Is an infrequent complication which may required treatment with Insulin and/or hypoglycemic agents.

Growth problems
Stunted growth is common in thalassemia patients.

Contributing factors
Many factors have been implicated to short stature; including chronic anemia, hypersplenism and folate deficiency.

Chronic liver disease, zinc deficiency, undernutrition and psychosocial stress are nonendocrine additional factors that can contribute to stunted growth.

Management
Replacement therapy with growth factor may be needed

Osteoporosis
➢ Fractures often secondary to mild or moderate trauma.
➢ Osteopenia

Management
✓ Calcium and vitamin D supplements.
✓ Bisphosphonates.

Eyes & ears
➢ Retinal pigmentary changes
➢ Cataract
➢ abnormal electroretinographic potentials

Management
✓ Oral iron chelators
Pseudoxanthoma elasticum

Pseudoxanthoma elasticum (PXE) has been reported to be one of the complications of thalassemia

Management

A magnesium carbonate- containing phosphate binder.

Thromboembolic complications

Increased risk of venous and arterial thrombosis.

Management

✓ Platelet anti-aggregating agents for patients with thrombocytosis.

✓ Low-molecular-weight heparin followed by long-term oral anticoagulants is recommended for patients with a history of thrombosis and in all patients before surgery and during pregnancy

Infections

Bacterial infections represent the second most common cause of death in thalassemia major and a main cause of morbidity.

Predisposing factors include splenectomy, iron overload and the use of DFO

Ferrophilic organisms such as Yersinia and Klebsiella are common pathogens.

Recommended chemoprophylaxis: for the prevention of post splenectomy infections include Antibiotic prophylaxis with penicillin, amoxicillin or erythromycin for the first 2 years after surgery and for children until age 165 years, as well as early antibiotic treatment for fever and malaise.

Vacccinations: Immunization against S. pneumoniae, H. influenzae and meningococcal disease is also recommended.

Gallstones

If stones are present at the time of splenectomy, cholecystectomy should be performed at the same time.

Complication due to Extramedullary erythropoiesis

➢ Paraparesis and
➢ cauda equina syndrome
Management

✓ Chelation
✓ Maintenance of Hb level
✓ Hydroxyurea
✓ Surgery is limited to selected cases.

Nutrition:

Nutritional deficiencies are common in thalassemia, due to hemolytic anemia, increased nutritional requirements, and morbidities such as iron overload. Dietary iron restriction has long been the focus of nutrition intervention in thalassemia patients. Several studies that were conducted on nutritional status of thalassemia patients revealed the fact that thalassemia patients have reduced intake of many essential nutrients including vitamin A, D, E, K, folate, calcium and magnesium. Moreover, different studies also demonstrated decreased circulating essential nutrients and the prevalence of much co-morbidity with nutritional linkages in patients with thalassemia. So, optimizing dietary intake through nutrient dense foods and appropriate use of supplementation where necessary may improve overall health of the thalassemia patients.

Patients need to be evaluated annually by anthropometry by the care giver regarding adequate dietary intake of calcium, vitamin D, folate, trace minerals (copper, zinc, and selenium) and antioxidant vitamins (E and C).

1. For non-transfused thalassemia patients (NTDT): a moderately low-iron diet is encouraged—that is, avoiding only iron-fortified cereals and other products and excessive consumption of liver and red meat. Take at least one glass of milk daily as it helps to prevent osteoporosis; and Drink black tea with meals to reduce iron absorption from food.

It is difficult to avoid taking non-meat iron because it is present in most foods. Non-meat iron is present in eggs, cereals, vegetables, fruits roots (potatoes, parsnips), beans and lentils. However, diet can be modified by taking more of the foods which decrease and less of the foods which increase the amount of iron absorbed into our body. The foods which decrease its absorption are: (i) Cereals; and (ii) Dairy products. The foods which increase its absorption are: Fruit and vegetables rich in Vitamin C, meat, fish, and poultry. So, Vitamin C which is present in fruits, such as lemon, guava, orange and orange juice should be taken separately, rather than with main meal as these are good sources of antioxidants which are very much necessary for thalassemia patients.
2. For regularly transfused patients on chelating therapy, a **low-iron diet is unnecessary** and may decrease the quality of life for some patients.

3. There are some nutrients that thalassemia patients need in greater amounts
   
i) **Folic acid:** For all thalassemia major and intermediary patients’ regular folate supplementation is recommended;

   ii) **Zinc:** Regarding zinc it is an essential nutrient that has been shown to be particularly beneficial to immune status, bone health and growth in thalassemia. So,

   iii) **Vitamin D:** In several studies Vitamin D insufficiency is reported in the majority of thalassemia patients in the USA and elsewhere. The risk of vitamin D deficiency increases with age, and older thalassemia patients have significantly worse vitamin D status compared with age-matched healthy controls. So,

       (a) If vitamin D level is less than 20ng/ml then regular/daily vitamin D supplement (1000 IU/d) or a high dose infrequent vitamin D supplement (50,000 IU dose every 3-4 weeks at time of transfusion) is recommended.

   iv) **Vitamin E:** Several studies demonstrated that Vitamin E values are depressed in thalassemia owing to increased consumption of this vitamin as thalasemia patients are at increased risk of oxidative stress. **Vitamin E is therefore often suggested for thalassemia patients specially who has secondary hemochromatosis.**

   v) **Vitamin C:** Thalassemia major patients are allowed only minimum levels of vitamin C daily because it liberates iron into the blood stream.

**Genetic Counselling:**

**Definition of Genetic Counseling**

➢ Genetic counseling is the communication process of providing information and support to individuals and families with a diagnosis and/or risk of occurrence of an inherited disorder.

➢ Genetic counseling is an integral and necessary component of comprehensive care for patients and parents affected by all forms of thalassemia disease and trait.

For successful genetic counselling:

- A correct diagnosis is necessary
- Explanation of the nature and prognosis of the disorder and treatment available and where to find it.
- Estimation of genetic risk for parents and family members.
- Communication of genetic risks and options for avoiding them including the chances of parents and other family members passing the disorder on to their children.
• The options for avoiding further affected children must also be addressed, including technique of prenatal diagnosis and associated problems.
• Supporting the individual or couple in making the decision that is right for them is also part of counseling.

When Genetic counseling is needed:
• At diagnosis and during adolescence
• prior to and after any genetic testing
• prior to pregnancy and/or as early in pregnancy as possible
• Annual follow-ups are needed to reinforce teaching.
• If you and your partner both have thalassemia trait, for each pregnancy, there is a:
  o 25% chance that the child will have thalassemia disease
  o 25% chance that the child will have normal hemoglobin
  o 50% chance that the child will have thalassemia trait
Patient Record Book:

cÖ‡MÔm wi‡cvU©

ZvwiL: mieivnK…Z i³ I cwigvY:

D’PZv- ‡mwg, IRb- †KwR, gv_vi cwiwa- i³ cwimÂvjbj †bvU:
eywxweKvk (I Q test) - ‘šÍ-

General Test:

CBC:
Coombs (Indirect): Coombs (Direct):

HLA typing:

Iron and Toxicity Test:
S.Ferritin: TIBC:

Liver Function Test:
G/E

AST: ALT: HBV:
HCV: HIV: Syphilis: Chelating agent:

S. Bilirubin: Total Albumin:

Malaria Parasite: i³ cwimÂvjbRwbZ ZvrýwYK
cvk¡ćOwZwµqv I wPwKrmv:

Spleen: G/E
Heart: G/E

Endrocrine Test:

Ionized Calcium: Fasting Glucose:
FSH: Estradiol: cieZÇx wfwR†Ui ZvwiL
Avwg Wvt 

‡Kgb AvQ Zzwg?

Avwg ‪Zvgvi mv‡_ K_v ej‡Z PvB|

‡Zvgvi wK Ki‡Z fvj jv‡M?

‡Zvgvi gZ wkï‡`i ‪QvU‡ejv ‪_‡K G KwU AmyL n‡Z cv‡i hvi bvg Ô_¨vjv‡mwgqvÔ| GwU i‡³i G KwU AmyL hvi Kvi‡Y kvixwiK wKQz Amyweav nq|

‡Zvgvi wK ‪ekxifvM mgq Lvive jv‡M?

A‡bK mgq `~e©j jvM‡Z cv‡i, hvi KviY kix‡i i³ K‡g hvIqv (i³k~Y¨Zv)| wKš †Zvgvi ‪hme ‪Ljv fvj jv‡M ‪m,wj Zzwg ‪Lj‡Z cvi| ‪Lv‡g jv‡M jv‡M ‪m,‡K GwU Amy‡Li Rb¨ DcKvix|

‡Zvgvi Amy‡Li Rb¨ ‪Zvgvi covïbv, eÜZ‡i mv‡_ mgq KvUv‡bv, Mvb Kiv, eB covmn Ab¨vb" fvjjMvi KvR,wj Zzwg Ki‡Z cvi ‪Zvgvi‡K wbqwgZ cywôKi Lvevi, djk~j, `ya BZ¨vw" ‪L‡Z n‡e| wKQz Lvevi hvi g‡a” Avqi‡bi cwivyY ‪ekx ‪mme ‪hgbt KwjRv, Kjv bv Lvlqv fvj| Pv ‪Lj‡j G‡j‡j‡M wKQz myweav cvlvq hvq| ‪Zvgvi fvj jvM‡j Pj I wPwb Qvov we~zU ‪L‡Z cv‡iv| A‡bK mgq ‪Zvgvi G Amy‡Li Rb¨ ‪Zvgvi wbqwgZ i³ ‪bqv jvM‡Z cv‡i Ges ‪mB mv‡_ wKQz Jla wbqwgZ ‪mbeb Ki‡Z n‡e|

miKvix wPwKrmv‡mev,wj ‪h,‡jv ‪Zvgvi nv‡Zi Kv‡Q ‪q‡Q ‪mLvb ‪_‡K (‡hgbt Dc‡Rjv ~v”°” Kv‡c| ‪Rjv nvmcvZvj, ‪gwW‡j K‡jR I nvmcvZvj) Zzwg wPwKrmv‡mev ‪c‡Z cv‡iv ‪Kv‡bv we‡kl wPwKrmv ‪mev (Acv‡ikb, ‪eb g¨v‡iv UvÝcøvb‡Ukb, BZ¨vw”) Avgiv ‪Zvgvi I cwiev‡i mv‡_ Av‡jvPbv K‡i wm×vŠl wbe|

Avwg ‪t welq,wj D‡jøL Kijvg ‪m,wj ‪g‡b Pj‡j Zzwg Ab” wkï‡`i gZ ~vfweKfv‡e Rxeb hvcb Ki‡Z cvi‡e| Avwg ‪Zvgvi my ~” I my> i fwel”r Kygbv Kwi|

ab¨ev`
Prevention of Thalassemia:

Thalassemia is a preventable disease. Creating awareness, population screening, avoiding marriage between carriers, genetic counseling and preventing birth of affected fetus by prenatal diagnosis can eliminate Thalassemia from our country. Many countries in the world had controlled Thalassemia by mandatory carrier screening. The high risk couples should be identified at the primary health care level and be referred to a regional/tertiary, well equipped center for proper management.

1. Creating awareness
   • Creating awareness about Thalassemia to the general population, government and medical communities by holding seminars, workshops and writing articles in the daily newspapers, broadcasting in television and radio is of prime importance.
   • The government must also take steps to create awareness among the rural populations by involving thana health complexes and other different local organizations through different activities like seminars, symposium, publications etc.

2. Population screening
   
   (A) Screening High Risk Family Members
   The family members of couple having Thalassemia child are the high risk group. After proper counseling they should be screened for carrier status.

   (B) Child bearing potential group screening:
   • As the prevalence of Thalassemia carrier is high in our country, the future parents in the general people should be screened for detection of carrier status.
   • It can be started from school, college, university or community level

   (C) Premarital Screening:
   Before marriage, the bride grooms should be screened to detect carrier status. Marriage between two carriers should be discouraged.

   (D) Screening of pregnant mothers at first visit:
   • All pregnant mothers should be routinely screened out to find out carrier status of Thalassemia.
   • If the pregnant lady is detected as a carrier, her husband should be screened out immediately.
   • If both husband and wife are detected as carriers, only then they should be offered prenatal diagnosis after proper counseling.
3. Genetic counseling

- Genetic counseling plays the most important part in thalassemia prevention program.
- Genetic counseling offered to couple when both are carrier of Thalassemia or already have a child with Thalassemia.
- They are counseled about the future pregnancy, risk of having affected children, available prenatal diagnosis, cost, result and consequences.

4. Prevention of Birth of new Thalassemia baby

- Prenatal diagnosis is a hope of Thalassemia carrier couple to confirm a healthy baby before birth.
- Birth of new Thalassemia major babies can be prevented by terminating the affected fetuses confirming by prenatal diagnosis.

Screening method:

The most feasible screening can be done by RBC indices through CBC test. The MCH & MCV parameters will be carefully looked out in CBC report of an individual.

- With or without anemia, When the CBC report of an adult person will show MCV is ≤ 80 fL or MCV ≤ 27 pg, it indicates to be Thalassemia carrier or iron deficiency anemia or others causes of microcytic anaemia
- They should be offered Hb Electrophoresis test to confirm Thalassemia trait/carrier or not.

If the Hb Electrophoresis report is normal, they should be treated with Iron for 2 weeks to see the response.
Carrier detection:

Identification of asymptomatic carrier:

i) Beta thalassemia trait, ii) Hemoglobin E trait and iii) Homozygous hemoglobin E (Hb E disease)

Flow chart using routine CBC, Electrophoresis (and serum ferritin optional) is given.

*To be able to differentiate HbA2 from HbE.
**Pre-natal diagnosis** (diagnosis before birth):

Genetic analysis from Amniotic fluid (by amniocentesis) and Chorionic villus (by chorionic villus sampling) is the mainstay of prenatal diagnosis of Thalassemia.

**Amniocentesis:**

- Amniocentesis is the process of collecting amniotic fluid from the womb under the guidance of real-time ultrasound.
- It is done at 15 to 18 weeks of pregnancy when the size of the fetus is about 1.5 to 2 inches.
Chorionic Villus Sampling (CVS):

- Chorionic villus sampling is the process of collecting placental tissue from the womb.
- It is done at 11 to 14 weeks of pregnancy, earlier than amniocentesis. At this stage the size of the fetus is about 1 to 1.5 inch.
- There is only 0.5 to 1% risk of abortion in amniocentesis or Chorionic Villus sampling procedures.
- Both the amniotic fluid and chorionic villi collected in those procedures along with parent’s blood are sent to laboratory for genetic analysis. It takes 1 to 2 weeks to get the result.
- When the result is that the fetus is affected by Thalassemia major, the physician counsel the parents to take the decision to continue or discontinue the pregnancy according to social, religious and legal issue.
I. Primary haematology tests

- Full medical history and family history
  Complete blood cell count with erythrocyte indices
  Blood smear/BCB staining

  - Low MCV (<80 fl) +
  - Low MCH (<27 pg)

  - Microcytosis
  - Hypochromia
  - Target cells
  +/− Inclusion bodies (Hb H)

  Serum ferritin >12 ng/mL → Hb electrophoresis & HPLC

  Serum ferritin <12 ng/mL → Other causes of anemia?

  Consider iron deficiency anemia

  Adequate iron supplement for 3 months

  No improvement

II. Type of thalassaemia

  - HbA₂ ≥ 4%
    - HbF 0.1-5%
    - HbA₂ < 4%
      - HbF < 1%
      - HbF > 5-50%
    - Hb A₂ < 4%
      - Hb CS/FP
      + Other normal Hb variant

  - Hb H disease
  - Hb E disorders
  - Hb S disorders
  - Hb C disorders
  - Others

III. Genetic testing

- DNA analysis for α- and β-globin mutations
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- Patrou M.: Prevention of Thalassaemia and Other Haemoglobin Disorders: Volume 1: 2nd edition. Editor: John Old,*Thalassaemia International Federation*


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