State of Thalassemia in Bangladesh: A Review

By

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A thesis submitted to the Department of MNS in partial fulfillment of the requirements for the degree of Bachelor of Science in Microbiology

Department of Mathematics and Natural Sciences

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Declaration

It is hereby declared that

1. The thesis submitted is my own original work while completing degree at BRAC University.
2. The thesis does not contain material previously published or written by a third party, except where this is appropriately cited through full and accurate referencing.
3. The thesis does not contain material which has been accepted, or submitted, for any other degree or diploma at a university or other institution.
4. I have acknowledged all main sources of help.

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Approval

The thesis (review paper) titled "State of Thalassemia in Bangladesh: A Review" submitted by

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of 12th semester, 4th year has been accepted as satisfactory in partial fulfillment of the requirement for the degree of B. Sc. in Microbiology on 30th January, 2019.

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Ethics Statement

The review paper titled “State of Thalassemia in Bangladesh: A Review” has been composed by Md. Shariqul Islam Reedoy where no false information has been inserted. All the information provided in this article have properly been cited. The confidentiality of all those reference sites have been maintained by paraphrasing those data in the paper. All the tables, pictures, charts have been cited. Apart from this, all the rules and regulations have been followed in composing the paper.

Abstract

This dissertation investigates what thalassemia is all about, what types of thalassemia there are seen, the causes of thalassemia and signs and symptoms of this disease. This article provides an overview of thalassemia in South-East Asia mainly focusing on Bangladesh. It describes how thalassemia has been encroaching across the region, it's impact on the health concern of the inhabitants of this region. Most importantly, how the impact of this disease can be checked. The diagnosis, treatment procedure to cure patients from this disease have been analyzed. Along with this, this article discusses our government can take assess the thalassemia condition throughout our country and take measures to stop this as soon as possible before it gets out of our control.

Key Words: Blood disorder; Genetic inheritance; Epidemiology; Treatment; Mutation profile; Recommendation.

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List of Acronyms

i) **RBC (**Red Blood Cell**)**
ii) **WHO (**World Health Organization**)**
iii) **HbE (**Hemoglobin E**)**
iv) **HbA1 (**Hemoglobin, alpha 1**)**
v) **HbA2 (**Hemoglobin, alpha 2**)**
vi) **HbH (**Hemoglobin H**)**
vii) **WBC (**White Blood Cell**)**
viii) **MCV (**Mean Corpuscular Volume**)**
ix) **MCH (**Mean Corpuscular Hemoglobin**)**
x) **MCHC (**Mean Corpuscular Hemoglobin Concentration**)**
xi) **RDW (**Red blood cell Distribution Width**)**
xii) **CBC (**Complete Blood Count**)**
xiii) **CVS (**Chorionic Villus Sampling**)**
xiv) **PCR (**Polymerase Chain Reaction**)**
xv) **GVHD (**Graft Versus Host Disease**)**
xvi) **HbS (**Sickle cell Hemoglobin**)**
xvii) **HbD (**Hemoglobin D**)**
xviii) **TDT (**Transfusion Dependent Thalassemia**)**
xix) **NTDT (**Transfusion Dependent Thalassemia**)**
xx) **HCV (**Hepatitis C Virus**)**
xxi) **HBV (**Hepatitis C Virus**)**
xxii) **BMT (**Bone Marrow Transplantation**)**
xxiii) **PND (**Prenatal Diagnosis**)**

State of Thalassemia in Bangladesh: A Review

STATE OF THALASSEMIA IN BANGLADESH: A REVIEW

Abstract:

Thalassemia is a group of genetic, congenital disorders of the blood. More specifically, it is a disorder of the hemoglobin molecule which is found in red blood cells. The color of RBC is red due to the presence of the hemoglobin molecule. Thalassemia has been the most common genetic blood disease in the globe so far and differs within different population groups. This threat has been developing as a global public health concern.

According to the World Health Organization (WHO), a minimum of 6.5% of the global populations are carriers of different inherited disorders of hemoglobin molecules. South Asia is considered worldwide as a hotspot of hemoglobinopathies (Colah R, Gorakshakar A, et al., 2010), which is the home to 23% of the world's population numbered around 1.7 billion people. Maximum information regarding thalassemia in this South Asian area derives from studies operated in India. Because of extreme heterogeneity, an uneven frequency of β-thalassemia heterozygote or carrier in the range of 1 and 10% has been stated throughout several areas of India (Colah R, Gorakshakar A, et al, 2010). However, the general occurrence of β-thalassemia carriers has been estimated to remain between 2.78 and 4% within India (Mohanty D, Colah RB, et al, 2013). This means there are 30–48 million beta-thalassemia carriers approximately in India and around 5–12 million carriers in Pakistan with a carrier rate of 5–7% (Colah R, Gorakshakar A, et al, 2010).

World Health Organization (WHO) also presumes that there are nearly 3% beta-thalassemia carriers and almost 4% Hb E/beta-thalassemia carriers present in Bangladesh. In Bangladesh, over 14000 children are born with thalassemia every year (Khan W. A., 2019). Most of them are born in countries with limited resources where priority leans towards facing high rates of infant and child mortality from infectious diseases and malnutrition (Olivieri NF, Pakbaz Z, et al., 2011). The patients who are suffering from β-thalassemia major and Hb E/ β-thalassemia do not survive for over 5 years without blood transfusion. We have also discussed the preventive policies of thalassemia from the situation of Bangladesh which could be operative for other developing countries. Due to the high rate of international migration, thalassemia is spreading to non-endemic parts of the world (Colah R, Gorakshakar A, et al., 2010). In many Asian countries, the most common form of thalassemia results from the coinheritance of beta-thalassemia and HbE.

In this wide-ranging review, the goal is to demonstrate the epidemiological aspects of thalassemia, mutation profile and current treatment and management practices in the country by sharing the experience of dealing with 1178 cases over 2009–2014 time periods within a specialized thalassemia treatment center (Hossain M S., et al., 2017).

STATE OF THALASSEMIA IN BANGLADESH: A REVIEW

Introduction:

Thalassemia has become the most common congenital disorder in Bangladesh. It has been a growing concern in this country throughout the last decade. According to a study operated in 2015, thalassemia occurred in approximately 280 million people and among them, 439,000 were having an acute disease ("Thalassemia," n.d.). Thalassemia causes men and women to suffer similarly and happens in nearly 4.4 of every 10,000 live births. It is most common among people of Greek, Italian, South Asian, Middle Eastern, and African descent.

Both females and males possess identical rates of disease. Thalassemia is responsible for 16,800 deaths only within 2015, plummeting from 36,000 deaths in 1990 ("Thalassemia," n.d.). People who possess minor degrees of thalassemia, adjacent to those with sickle-cell trait, have some defense against malaria, demonstrating why they are more common in regions of the world where malaria exists (Weatherall, D. J., 2015). Every year among all the babies born with thalassemia disorder, researchers assume that 100,000 are born with acute forms of thalassemia on average throughout the world.

What is Thalassemia?

Thalassemia is known to be a blood disorder that is genetically inherited and results from abnormal Hemoglobin production. Hemoglobin is the protein molecule present in our red blood cells responsible for transmitting oxygen towards the cells. If Hb production is obstructed it can put our body into danger. This blood disorder is capable to create severe anemia (a condition where the body doesn't contain enough RBCs). It is genetically inherited from a person's parents. Two major types of thalassemia are seen namely alpha thalassemia and beta thalassemia. In alpha-thalassemia, the α-globin chain gets mutated and on the other side in the case of beta-thalassemia, the β-globin chain gets mutated. Only one gene on chromosome 11 encodes the β-globin chains and two closely linked genes lying in chromosome 16 encode α-globin chains. As the number of missing genes among the two gene loci for alpha-globin or one gene locus for beta-globin increases the α and β thalassemia disease get much more deleterious respectively. Following an autosomal recessive manner, both α- and β-thalassemia are often genetically inherited. Incidences of dominantly inherited α- and β-thalassemia have been informed, the first occurrence was of an Irish family with two deletions of 4 and 11 base pairs in exon 3 interrupted by an addition of 5 base pairs within the β-globin gene. For the autosomal recessive forms of the disease, both parents must be carriers for a child to be affected. If both parents possess a hemoglobinopathy (only one allele is normal and the other one is mutated) trait, there is a 25% possibility in every pregnancy to have a child affected by thalassemia.

Types of Thalassemia:

Based on the number of missing genes thalassemia are classified as well:

Alpha Thalassemia

Firstly, as two genes (consist of four alleles; two of which come from mother and two of which from father) named HBA1 and HBA2 are responsible for the production of alpha-globin chain, there are four types of alpha-thalassemia can be possible (Galanello, Renzo; Cao, Antonio, 5 January 2011). Alpha-thalassemia can result in the reduction of alpha-globin production, consequently less alpha-globin chains are synthesized, causing a high level of β chains in adults and γ chains in newborns. This high level of β chains produce unstable tetramers (called hemoglobin H or HbH of 4 beta chains), which have abnormal oxygen dissociation curves. Alpha thalassemia is often observed in the people of Southeast Asia, the Middle East, China and in those of African descent ("Thalassemia," n.d.).

No. of missing genes	Types of alpha thalassemia	Symptoms
1	Silent carrier	No symptoms
2	Alpha thalassemia trait	Minor anemia
3	Hemoglobin H disease	Mild to moderate anemia may lead a normal life
4	Hydrops fetalis	Fetal death usually occurs at birth

Beta Thalassemia

Secondly, since only one gene (consist of two alleles) named HBB on chromosome 11 in the human genome is responsible for beta-globin chain production inherited in an autosomal recessive manner. The severity of the beta-thalassemia depends on the nature of the mutation and the presence of mutations in one or both alleles.

The condition of both alleles determines the possible clinical picture:

- β thalassemia major (Mediterranean anemia or Cooley anemia) is caused by a β^o/β^o genotype. No functional β chains are produced, and thus no hemoglobin A can be assembled. This is the most severe form of β-thalassemia;
- β thalassemia intermedia is caused by a $\beta^+/\beta o$ or β^+/β^+ genotype. In this form, some hemoglobin A is produced;
- β thalassemia minor is caused by a β/β^o or β/β^+ genotype. Only one of the two β globin alleles contains a mutation, so β chain production is not dreadfully compromised and patients may be relatively asymptomatic.

Beta thalassemia most often occurs in the population of Mediterranean origin. To a lesser extent, Chinese, other Asians, and African Americans can be affected.

("Thalassemia," n.d.)

Delta Thalassemia

Among all the hemoglobin molecules persisting in our RBCs, around 3% of adult hemoglobin are observed to be made up of α and δ chains with the rest being α and β chains. It is observed in some cases that if the HbA gene is mutated, it can result in incapacity to produce delta chain ultimately causing delta thalassemia.

("Thalassemia," n.d.)

Combination hemoglobinopathies

Thalassemia can coexist with all other hemoglobinopathies. The most popular among these are:

- Hemoglobin E/thalassemia: This kind of blood disorder is mostly observed within the people of Thailand, Cambodia and some parts of India which has been identified as β thalassemia major or thalassemia intermedia.
- Hemoglobin S/thalassemia: This blood disorder is predominantly observed in the inhabitants of the African and Mediterranean region, is identical to sickle-cell anemia, as well as they are possessed with splenomegaly (abnormally large size of spleen).
- Hemoglobin C/thalassemia: This blood disorder has been most popular in Mediterranean and African populations, hemoglobin C/βo thalassemia causes a moderately severe hemolytic anemia with splenomegaly; hemoglobin C/β+ thalassemia generates a milder disease.
- Hemoglobin D/thalassemia: Hemoglobin D/thalassemia mostly prevails in the residents of north-western parts of Pakistan and India (more specifically Punjab region).

Signs and symptoms:

- **Iron overload:** People having thalassemia can suffer from an excess of iron in their bodies, either from the disease itself or from blood transfusions frequently. Having excessive iron can cause damage to the heart, liver, and endocrine system, which includes glands that generate hormones and by doing so regulate several processes throughout the body. The damage is branded by excessive deposits of iron. Without a satisfactory level of iron chelation therapy, almost all patients having beta-thalassemia deposit potentially fatal iron levels (Cianculli P., 2011).

- **Infection:** Patients suffering from thalassemia possess a high risk of infection. This is specifically factual if the spleen has been detached from the body.

- **Bone deformities:** Thalassemia can cause augmentation of the bone marrow, which resulting bones to widen. This can ultimately result in abnormal bone structure, especially in the face and skull. Bone marrow expansion also makes bones thin and brittle increasing the danger of broken bones.

- **Enlarged spleen:** The spleen supports to fight infection and sieves undesirable material, for example, old or damaged blood cells. Thalassemia is frequently accompanied by the destruction of a huge number of red blood cells and the job of eliminating these cells causes the spleen to enlarge. Splenomegaly can further deteriorate the consequences of anemia and it can decrease the life of transfused red blood cells. If the spleen gets too large then it must be surgically detached from the patient's body.

- **Slowed growth rates:** Anemia can slow down a child's growth. Thalassemia can delay the appearance of puberty in the patient. (Soliman, Ashraf T, Kalra, Sanjay, De Sanctis, Vincenzo, 2014).

- **Heart problems:** Severe thalassemia can also become responsible for diseases like congestive heart failure and abnormal heart rhythms.

- Children can begin demonstrating hints of thalassemia during the first two years of their life. Some of the most obvious signs seen include fatigue, jaundice, pale skin, poor appetite, and slow growth.

- Fussiness or paleness of the face, poor appetite or jaundice (where the skin of the body and white portion of the eye turns to yellow) can be indications for mild thalassemia.

Effect of thalassemia on pregnancy:

Pregnancy is a vital time for a woman. A good pregnancy can provide us with a healthy and beautiful child. Thalassemia can hamper a woman related to pregnancy. The genetic disorder harms reproductive organ development. As a result, a woman having this issue may face fertility difficulties. To avoid such circumstances, a woman must consult with a doctor whether she is in the best condition to conceive a baby. The iron level of the mother must be checked in a regular interval. Preexisting issues like damage to the major organs are also considered with utmost priority.

Prenatal testing for thalassemia can be done at 11 or 16 weeks. This is conducted by collecting fluid samples from either the placenta or the fetus, respectively.

Pregnant mothers carry some risk factors which are mentioned below:

- ✓ A higher risk for infections
- ✓ Gestational diabetes
- ✓ Heart problems
- ✓ Hypothyroidism, or low thyroid
- ✓ Increased number of blood transfusions
- ✓ Low bone density.

Diagnosis:

Hb Electrophoresis Test

To diagnose thalassemia, one first needs to collect a blood sample from the person's body. A phlebotomist collects blood samples through venipuncture procedure. After the collection of blood samples, it is put under a complete blood count diagnostic machine, the machine provides us exact amounts of blood cells (such as RBC, WBC, platelets, Hb, MCV, MCH, MCHC, RDW, etc). This test acts as an indication for us to judge a person's health state. If we observe a very low number of red blood cell then it makes us sure that the corresponding person is inflicted with anemia. Here, if the MCV value is less than 80 then the patient is either carrier or patient. Again, if the MCH value is ~28 then the patient seems to be normal otherwise he/she is a patient.

The following table shows the normal blood count cell results for adults:

CBC: compete blood count reference ranges

Blood component	Abbreviation used	Reference range	SI Reference range
White blood cells	WBC	4500-11,000/mm^3	4.5-11.0 x 10^9/L
Red blood cells*	RBC	Male: 4.3-5.9 million/mm^3 Female: 3.5-5.5 million/mm^3	Male: 4.3-5.9 x 10^{12}/L Female: 3.5-5.5 x 10^{12}/L
Hemoglobin*	HGB	Male: 13.5-17.5 g/dL Female: 12.0-16.0 g/dL	Male: 2.09-2.71 mmol/L Female: 1.86-2.48 mmol/L
Hematocrit*	HT	Male: 41%-53% Female: 36%-46%	Male: 0.41-0.53 Female: 0.36-0.46
Mean corpuscular volume	MCV	80-100 μm^3	80-100 fl
Mean corpuscular hemoglobin	MCH	25.4-34.6 pg/cell	0.39-0.54 fmol/cell
Mean corpuscular hemoglobin concentration	MCHC	31%-36% Hb/cell	4.81-5.58 mmol Hb/L
Platelets	Platelets	150,000-400,000/mm^3	150-400 x 10^9/L

Figure: Blood cell count in healthy person

("Describe The Differences Between A Normal Patient's CBC and a Mystery Patient 1's CBC," n.d.)

After that, the blood sample is taken into the Hb electrophoresis machine. In the laboratory, the machine passes an electrical current through the hemoglobin in your blood sample. This causes the different types of hemoglobin to separate into different bands. In front of the monitor, we can see the graph demonstrating the percentage of different Hb proteins.

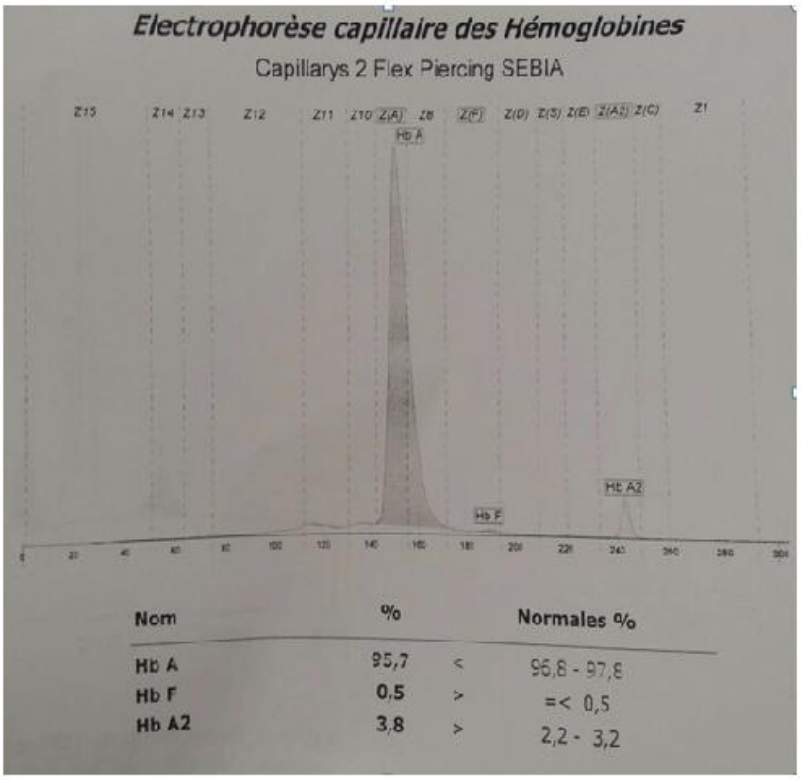

Figure: A report depicting Hb electrophoresis test result of a person

Then the blood sample is compared with the reference value to determine which types of hemoglobin are present. An experienced lab officer must operate this sensitive test.

After that, a report is published based on the result of the Hb electrophoresis machine.

Prenatal Diagnosis

Thalassemia detection is possible directly by the analysis of amplified DNA collected from fetal trophoblast or amniotic fluid cells. Nowadays, prenatal diagnosis by DNA analysis is available in the Mediterranean area (Cyprus, Sardinia, several regions of Continental Italy), Northern Europe (Netherland, Belgium, and Germany), Northern and South America, Hongkong, Taiwan, China, Indonesia, Malaysia, Jordan. Prenatal diagnosis service has also been introduced even in many developing countries. Fetal DNA analysis is done by one of the two methods described here. ("Medical Newsletter, Special Supplement," 2005)

1. **Chorionic villus sampling**: By needle insertion through the abdominal wall under ultrasound guidance, a small amount of chorionic villi material which is the same genetic makeup as the fetus is aspirated for DNA analysis. This is done around 10 weeks of pregnancy. CVS is preferable as it is done in the first trimester of pregnancy within the time limit laid down by abortion law in many countries. It also reduces the emotional stress of parents and complications of late termination of pregnancy.

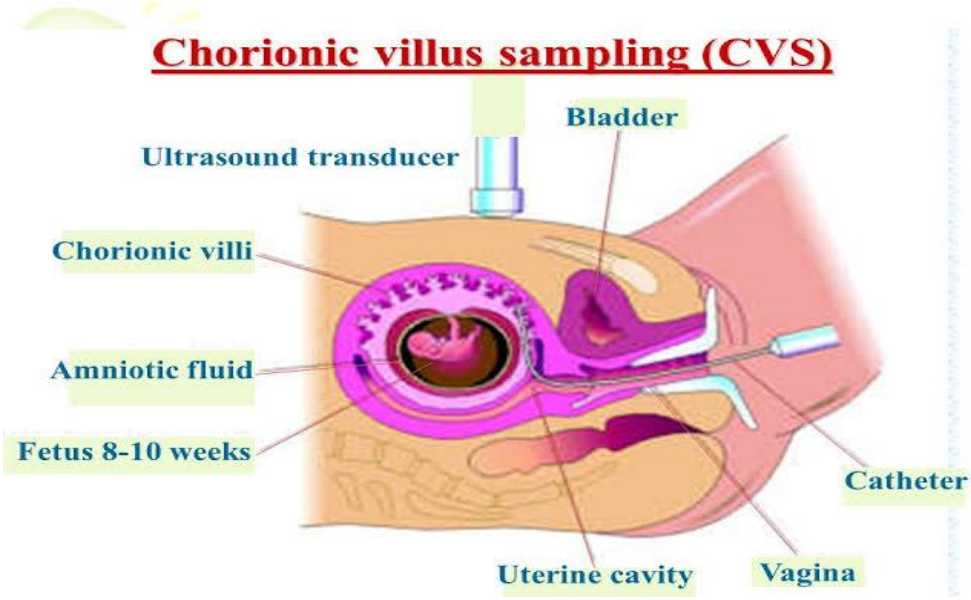

Figure: Chorionic Villi Sampling ("Prenatal Cytogenetic," 2020)

2. **Amniocentesis**: A small needle is injected through the abdomen under ultrasound guidance and about 15-20 ml of fluid from the amniotic cavity surrounding the fetus is aspirated for DNA analysis. This is done from 16 weeks of pregnancy.

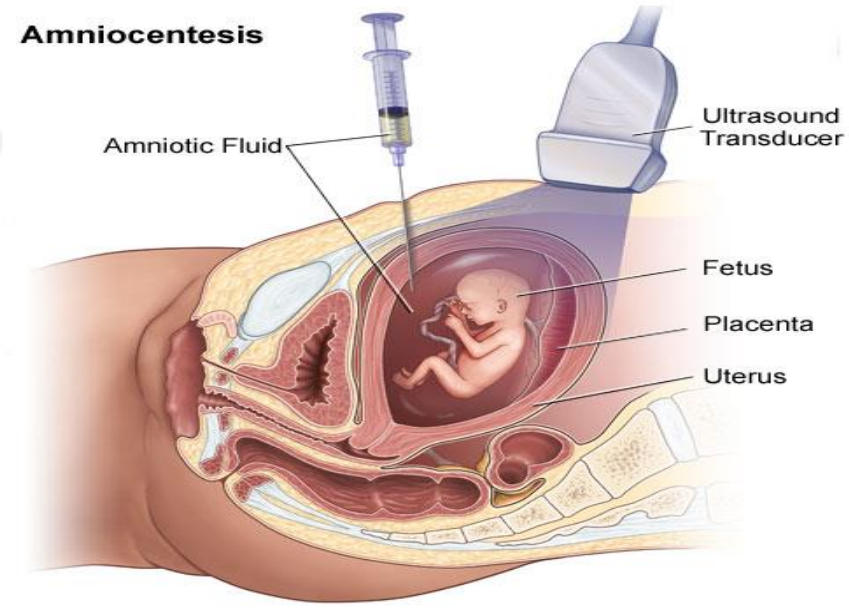

Figure: Amniocentesis ("New Study focusing on Prenatal Screening Test Market 2019-2025 Including Leading vendors," 2019).

Pre-implantation and Pre-conceptional diagnosis

Recent unique progress in molecular genetics to analyze the genotype of a single cell along with advancement in assisted reproduction techniques now made possible to detect Pre-implantation and Preconceptional diagnosis of thalassemia. It is performed either by biopsy of one to two blastomeres in eight-cell embryos after in vitro fertilization or by biopsy of trophectoderm cells from a blastocyst. Diagnosis is obtained by multiple nested PCR analysis to detect the mutations as well as polymorphic alleles at the β-globin cluster. Nowadays these techniques are widely available in continental Greece, Cyprus and also in China. Termination at this stage may diminish the moral, religious and emotional stress of the parents.

Treatment for thalassemia:

i) **Bone Marrow Transplant:** A bone marrow transplantation is known to be a medical procedure done to replace bone marrow that has been harmed or destroyed by disease, infection or chemotherapy. This surgical procedure involves transplanting blood stem cells, which traverse to the bone marrow where new blood cells are generated and help in the development of new marrow. Two types of bone marrow transplantation have been seen so far:

   a) **Autologous transplants:** In autologous transplants, a person's stem cell is utilized. They involve harvesting your cells before initiating a damaging therapy to cells such as chemotherapy or radiation. When the treatment is ended, the patient's cells are returned to his body. Autologous transplant is not available all the time. It can only be done if the patient has a healthy bone marrow. However, it decreases the possibility of some serious problems, including GVHD ("Types of Bone Marrow Transplants," n.d.)

   b) **Allogeneic Transplants:** In allogeneic transplants, cells collected from a donor are utilized. The person who donates those cells must be of a close genetic match to the patient who is receiving it. In maximum cases, blood relatives are chosen which seems to be the best option. Allogeneic transplants are essential if the patient (recipient) possesses a state that has harmed their bone marrow cells. However, they have a much more probability of certain complications, such as GVHD. In this case, the recipient needs to take some medications which help him to repress the immune system so that the new cells are not destroyed. This can lead the patient vulnerable to illness. The achievement of an allogeneic transplant depends on how thoroughly the donor cells match the patient ("Types of Bone Marrow Transplants," n.d.)

ii) **Blood Transfusion:** In thalassemia patient, a massive amount of red blood cells is destroyed. So, blood from a person should be transfused into a thalassemia patient whether it is minor or major thalassemia.

iii) **Removal of Spleen:** Spleen works as a filter to remove infection-causing microbial agents or damaged or unwanted blood cells. Thalassemia causes a great number of red blood cells to destroy. The task of removing a high number of RBC cause the spleen to be enlarged. The final condition is splenomegaly.

iv) Iron Chelation Therapy: When a thalassemia patient is gone through multiple blood transfusion procedures, iron gets overloaded in the patient's vital organs like kidney, liver, heart, etc. The deposition of a high number of irons causes those organs to damage. Therefore, iron chelation therapy is performed to remove excess iron from the body. To perform this therapy, some medications are applied like deferoxamine, deferiprone, or deferasirox.

- ✓ Deferoxamine is only effective via daily injections which makes its long-term use more difficult. It has the benefit of being inexpensive and decent long-term safety. Adverse effects are primary skin reactions around the injection site and hearing loss. The dose of deferoxamine is adjusted according to body iron load and age, and ranges from 20 – 40 mg/kg/day for children and up to 50 mg/kg /day for adults given for 8 – 12 hours for 5 – 7 nights per week (Sayani F., Warner M., Wu J., et al., 2008).

- ✓ Deferasirox has the advantage of being an oral medication. Common side effects include nausea, vomiting, and diarrhea. However, it is not effective in everyone and is probably not appropriate in those with significant cardiac issues related to iron overload. The cost of this medication is also higher than Deferoxamine. It has been approved for the treatment of chronic iron overload in patients with transfusion-dependent anemias aged 6 years or older and aged 2 – 5 years who cannot be adequately treated with deferoxamine. Dosing is adjusted based on the patient's transfusion rate and trend of iron load; treatment ranges from 10 – 30 mg/kg/day (Sayani F., Warner M., Wu J., et al., 2008).

- ✓ Deferiprone is a medication that is provided by mouth. Nausea, vomiting, and diarrhea are relatively common with its use. It is available in both Europe and the United States. It seems to be the most effective medication when the heart is significantly involved. Typical dosage is 75 mg/kg/d in 3 divided doses up to a maximum of 100 mg/kg/day (Hoffbrand VA, et al., 2002).

v) Other Medication and Supplement: Thalassemia can result in folic acid deficiencies. That is why doctors usually prescribe a 1 mg folic acid supplement daily. Naturally grown foods like dark leafy greens and legumes contain a high amount of vitamin B. Along with that thalassemia patients should avoid foods containing high iron levels like fish, meats, fortified cereals, breads, and juices. A low-fat, plant-based diet is the best choice for most people having thalassemia.

Figure: Legumes as folic acid supplement ("Foods rich in Folic Acid with supplements," n.d.)

Thalassemia: A Bangladesh Perspective:

Bangladesh has been one of the most populated countries in the globe, with a populace of more than 160 million people. More than 70% of the inhabitants of our country reside in highly resource-constrained rural areas, while most of the tertiary hospitals are situated in large cities, particularly in Dhaka (Rahman S, Ahmed T, Rahman AS, Alam N, et al., 2016). Government hospitals are often crammed with lots of patients and these institutions do not have sufficient medical resources (such as specialized and basic medical equipment, healthcare professionals and essential drugs). On the other hand, some private clinics and hospitals are comparatively resourceful but these are not open to the general population since the medical service expense is too much there. The treatment drop-out rate among a population afflicted with poverty is expected to be very high and is driven by lack of access, either due to lack of awareness or income of patients seeking care on the demand side or inadequate expertise, facilities, knowledge, and infrastructure from the supply side of health care.

In spite of Bangladesh being fallen in the world's thalassemia belt, the information on different aspects (epidemiology, clinical course, mortality, complications and treatment outcomes) of thalassemia is lacking. A comprehensive study has discovered that the higher occurrence of anemia in Bangladesh is not connected to iron shortage (Rahman S, Ahmed T, Rahman AS, Alam N, et al., 2016). The countrywide occurrence of anemia (33.1% in children below 5 years of age and 26% in women) was more than 3 times higher than that of iron deficiency in children (10.7%) and women (7.1%), indicating other decisive factors for this unprecedented scenario (Rahman S, Ahmed T, Rahman AS, Alam N, et al.; 2016). Another study has pointed out that nearly 28% of evaluated village women have been suffering from beta-thalassemia or HbE (Merrill RD, Ahmed Shamim A, Ali H, Labrique AB, et al.; 2012). Similar outcomes have been stated for women and children of the Southeast-Asian country like Cambodia which are likely to be inflicted with thalassemia (Karakochuk CD, Whitfield KC, et al.; 2015).

Because of significant achievement in the control of infectious diseases in Bangladesh, the child death rate has reduced by 71% as compared to that witnessed in the 1990s ("World Bank Country and Lending Groups," n.d.). Genetic disorders, specifically thalassemia, consequently seem to be a key public health concern in Bangladesh within the upcoming decades (Weatherall DJ, 2011).

Epidemiological study of thalassemia:

The available information on the commonness of hemoglobinopathies in Bangladesh is rare as population-based data in our country is not sufficient. World Health Organization (WHO) estimates that about 3% of the people of Bangladesh are the carriers of beta-thalassemia and 4% are the carriers of hemoglobin E (HbE) in Bangladesh ("Prevalence of diabetes and prediabetes and their risk factors among Bangladeshi adults: a nationwide survey," 2014). However, these estimates need to be interpreted with awareness since this information was mainly based on studies operated in 1980 and a small number of non-representative samples collected from treatment centers were analyzed (Weatherall DJ, 2010). The only published report obtainable on the prevalence of thalassemia among (n = 735) school children in Bangladesh demonstrated a 4.1% prevalence of the beta-thalassemia trait and a 6.1% prevalence rate for the HbE trait (Khan WA, Banu B, Amin SK, Selimuzzaman M, Rahman M, Hossain B, et al., 2005). An analogous study unveiled the regional variation of beta-thalassemia carriers starting from 2.9 to 8.1% and 2.4 to 16.5% for HbE carriers. The incidence of beta-thalassemia trait was almost alike within tribal children but the percentage of HbE carriers was much higher (41.7%). Another research with a small sample size also detected similar (39–47%) occurrence rate of HbE carriers among a tribal population in Bangladesh (Shannon KL, Ahmed S, Rahman H, Khyang J, Ram M, et al., 2015).

Bangladesh shares linguistic and socio-cultural similarities with the East Indian region, most commonly West Bengal in India. In general, the genetic makeup is also closely related in this part of the world despite different religious backgrounds (Eaaswarkhanth M, Dubey B, Meganathan PR, Ravesh Z, Khan FA, Singh L, et al., 2009). Hence, the occurrence of hemoglobinopathies in Bangladesh could be extrapolated from population-based studies conducted in West Bengal. A recent large population-based research (n = 50,487) in rural West Bengal discovered the frequency of beta-thalassemia carriers and HbE carriers to be 6.61 and 2.78% respectively (Mandal PK, Maji SK & Dolai TK, 2014). Another recent study (n = 9990) estimated the frequency of 3.64% for beta-thalassemia traits and 3.92% for the HbE trait (Mohanty D, Colah RB, Gorakshakar AC, Patel RZ, et al., 2013). Taking all these concerns into account, the predicted prevalence of beta-thalassemia carriers could be in the range of 3–6%, and 3–4% for HbE in Bangladesh.

It is a matter of concern that most of the children with severe forms of thalassemia (such as thalassemia major) usually die under 5 years of age and the average life expectancy of patients suffering from thalassemia is about 30 years, particularly in heavily resource-constrained countries (Modell B, Darlison M., 2008). Considering these factors, we can extrapolate the overall scenario of thalassemic patients in Bangladesh using data from West Bengal (Mandal PK, Maji SK, Dolai T, 2014). The number of patients suffering from thalassemia (β-major and HbE beta) with different levels of severity is estimated to be approximately 60,000–70,000 in Bangladesh (Weatherall DJ, 2010). With the birth rate of 21.6/1000, it could be predicted that nearly 2500 thalassemia major cases are added each year in Bangladesh (Mandal PK, Maji SK, Dolai TK, 2014). Due to considerable variation of thalassemia even within a population, micro mapping is essential to calculate the actual burden of thalassemia in Bangladesh.

Although malaria disease is highly rampant, contrary to the African region and certain parts of India, sickle cell hemoglobin (HbS) is not present at all in Bangladesh. Despite the fact that there

has been indication of a strong association in geographical distribution between malaria and HbS, the connection was found to be strong in only Africa but not in the America or in Asia (Piel FB, Patil AP, Howes RE, Nyangiri OA, Gething PW, Williams TN, et al., 2010). In India, the HbS variant is mostly limited to the hilly areas and Western region (Urade BP, 2013). As confirmatory diagnostic test (such as sickle solubility test) is not present in most of the diagnostic centers, it seems that some case of HbS could be misdiagnosed as HbD beta-thalassemia, which is comparatively a common type of hemoglobinopathy in Bangladesh and India.

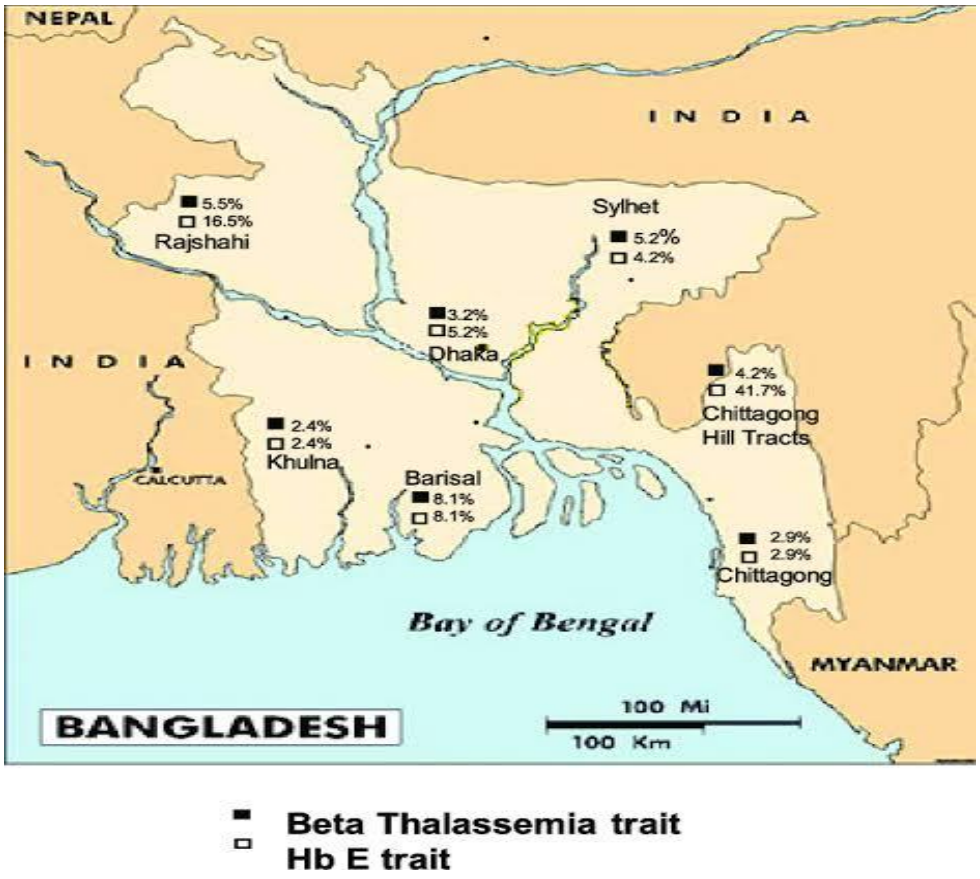

Figure: Map showing the distribution of β-thalassemia carrier & Hb E carrier in Bangladesh (Tahura S., Selimuzzaman M., Khan W. A., 2016)

STATE OF THALASSEMIA IN BANGLADESH: A REVIEW

Mutation profile of Thalassemia observed in Bangladesh:

The spectrum of mutations fluctuates across different topographical locations and cultures. Hence, the regional mutation profiling is important to take on any approaches (e.g. genetic counseling, prenatal diagnosis) to encounter thalassemia. Various mutations are connected with different types of thalassemia that affect the severity of the diseases. Mutations in globin genes (α or β) influence the synthesis of the globin chain that results in incomplete erythropoiesis. The diagnosis of α-thalassemia is often difficult and most cases (approximately 90%) remain as carriers among the populace of the Indian Subcontinent. Therefore, alpha thalassemia is beyond the scope of our present discussion (Panja A, Ghosh TK, Basu A., et al., 2012). More than 400 mutations or alleles have been stated for β-thalassemia.

Although there are a considerable number of thalassemia carriers present in Bangladesh, the genetic basis of thalassemia is undiscovered. Few molecular diagnostic laboratories are available in the country to pinpoint the mutations in the beta-globin gene. To the best of knowledge, there are only two reports exist on the mutation status of thalassemia in Bangladesh. A recent study (n = 256) showed prevalence of the five most common mutations including IVSI-5(G > C), Codon 41/42(-TCTT), Codon 8/9(G) codon 15 (G > A) and codon 30 (G > C), where IVSI-5 was found to be the most common in Bangladeshi patients (39.1%) (Chatterjee T, Chakravarty A, Chakravarty S., et al., 2015). Another study demonstrates that (n = 16), IVS-I-5 (G > C) accounted for 56.25% (Ibn Ayub M, Khan W., et al., 2010). As expected and discoursed earlier, the mutation profile (five common mutations) of Eastern India (West Bengal) was detected to be analogous to that of Bangladesh, IVS I-5(G > C) being the highest form of mutation (71.4%), with Codon 30(G > C) and Codon 15(G > A) the second and third most common alleles (Verma IC, Saxena R, Kohli S. et al.; 2011). The 619 bp deletion mutation is less frequent in Bangladesh (0.8%) and Eastern India (Black ML, Sinha S, Agarwal S, et al., 2010).

Management practice of thalassemia in Bangladesh:

Standard thalassemia management consists of a multidisciplinary method including a range of areas including pediatric hematology, pediatrics, transfusion medicine, endocrinology, cardiology, dentistry, dieticians, psychology, psychiatry, social work along with a robust blood bank system and infrastructure (Hossain M S., et al., 2017). In developing countries like Bangladesh, these multidisciplinary expertise and support conveniences are not usually obtainable in most public hospitals and private clinics. Besides, overall health consciousness is meager among the general populace in Bangladesh and there is no organized patient referral system. As a result of inadequate access to healthcare, a considerable proportion of the thalassemic patients might die even without being aware of their disease conditions. There is no nationwide policy or national health insurance structure regarding thalassemia prevention adopted by the government in Bangladesh.

To represent the overall contemporary situation of thalassemia management practice in Bangladesh, the experiences gained from Thalassemia Foundation Hospital (TFH) are put in this review paper (Hossain M S., et al., 2017).

Transfusion practice

Thalassemia carriers (trait) are healthy and do not need blood transfusion practice. Non-transfusion dependent thalassemia normally includes HbE beta-thalassemia and beta-thalassemia intermedia that do not require blood transfusions in regular intervals for survival (Taher AT, Radwan A, Viprakasit V, 2015). However, in Thalassemia Foundation Hospital, it was observed that some diagnosed carrier patients admitted as TDT (37% cases) and NTDT (63% cases). Infection and shortage of iron specifically in reproductive-age females could compound the pre-existing anemia although these patients are not transfusion dependent. This could happen because of misdiagnosis and/or lack of consciousness among the clinicians in Bangladesh. Thalassemia intermedia (TI) is signified as a group of patients with β-thalassemia characterized by diverse clinical severity between transfusion-dependent thalassemia major and mild symptoms of beta-thalassemia trait. Majority thalassemia intermedia patients are homozygous and compound heterozygous for β-thalassemia (Viprakasit V, Tyan P, Rodmai S, Taher AT, 2014). In Southeastern Asia including the Indian subcontinent, the most common form of severe thalassemia results from the coinheritance of HbE and β-thalassemia trait. Depending on clinical severity, HbE beta-thalassemia could be classified into three categories: mild (15% cases), moderately severe (majority of HbE beta-thalassemia cases) and severe. Up to 50% of all patients with HbE beta-thalassemia represents clinical manifestations similar to those of beta-thalassemia major (Viprakasit V, Tyan P, Rodmai S, Taher AT, 2014). Due to extensive clinical diversity, the management of NTDT is often challenging. Diagnosis and management of NTDT mainly depend on clinical observations. In our study, over 62% of HbE beta-thalassemia patients were treated as TDT while about 28% were NTDT. This unprecedented higher proportion of transfusion-dependent HbE beta-thalassemia in Bangladesh might cause inaccurate or misdiagnosis of the severity of different clinical manifestations of thalassemia patients. It could also be attributable to using Hb level to determine the need for transfusion in HbE beta patients as opposed to using other criteria including growth failure, delayed puberty, splenomegaly, the propensity to thrombosis and pulmonary hypertension (Fucharoen S, Weatherall DJ., 2012). A complete mutation profile (DNA testing) before the beginning of treatment is supportive to determine the prognosis, appropriate therapy and family counseling (Hossain M S., et al., 2017).

Increased consciousness among clinicians is a qualification for proper diagnosis and management of non-transfusion dependent thalassemia. Several reports have recommended the limitation of Hb level as a clinical decision indicator for initiating transfusion-dependent management since there were only minor differences in Hb levels (1.8–2.6 g/dl) between the mildest and most severe forms of HbE beta-thalassemia (Taher AT, Radwan A, Viprakasit V, 2015). Apart from that, some

children with HbE beta-thalassemia were seen to adjust to lower levels of Hb and managed almost normal life without transfusion (Allen A, Fisher C, Premawardhena A, Allen S, Arambepola M, et al., 2010). In one observation conducted in Sri Lanka, approximately 42% (37/84 cases) of patients with HbE beta-thalassemia could be overturned from transfusion-dependent thalassemia to non-transfusion dependent thalassemia without any harmful medical conditions, advocating that many of these patients actually received unnecessary regular blood transfusion therapy (Hossain M. S., et al., 2017). Patients with NTDT sometimes could suffer from severe anemia due to acute infection, therefore, transfusion therapy is not recommended immediately after diagnosis of NTDT (Viprakasit V, Tyan P, Rodmai S, Taher AT. 2014). Despite this fact, patients are not dependent on regular transfusions for survival although transfusion therapy may provide significant clinical benefits for some patients if administered properly (Taher AT, Radwan A, Viprakasit V., 2015).

Other than the pathophysiological, psychological and financial burden, the regular arrangement of safe blood is one of the biggest hurdles faced by transfusion-dependent families in developing countries. In Bangladesh, 85% of collected blood is contributed by the patient's relatives and friends, while the rest (15%) is donated by voluntary blood donors ("Situation assessment of public and private blood centers in Bangladesh," 2012). Taking this into consideration, before starting transfusion therapy, accurate diagnosis should be a mandatory part of the thalassemia management practice in Bangladesh.

Infection

Transfusion-dependent thalassemia patients are in danger of developing post-transfusion hepatitis. Among these infections, hepatitis B and C are the most common. Since there is a lack of an effective vaccine against HCV and inadequate infection control strategies, HCV is considered a major public problem in low to middle-income countries (Papatheodoridis G, Hatzakis A., 2012). Approximately 180.5 million people are infected by HCV in the world, of which 54.4 million is in South Asia (Messina JP, Humphreys I, Flaxman A, Pybus OG, et al., 2015). Some researchers have testified the higher prevalence of HCV among multi-transfused thalassemia patients, starting from 3 to 67.3% (Ali I, Siddique L, Rehman LU, Khan NU, Iqbal A, Munir I, et al., 2011). Increased risk of HCV infection in β-thalassemia patients is mainly connected with median age, duration, and mean amount of blood transfused. No HIV cases were diagnosed in Thalassemia Foundation Hospital. In the case of HBV, 6 cases were positive among 523 tested cases who had a blood transfusion. In the present study, 28.3% of the tested cases (n = 247) who went on multiple transfusions were observed to be HCV (Hepatitis C virus) positive. Another previous research operated in Bangladesh also detected higher positive cases of HCV among multi-transfused thalassemia patients (Verma IC, Saxena R, Kohli S, et al., 2011).

Diseases types	n (%)	Median age (year) at diagnosis	Transfusion status #/n (%)		
			TDT	NTDT	Not required
Hb-E-beta thalassemia	910 (77.25)	3.5	522/840 (62.14)	238/840 (28.33)	80/840 (9.52)
Beta thalassemia major	173 (14.69)	0.58	172/173 (99.42)	1/173 (0.58)	0/173 (0)
Beta thalassemia trait	64 (5.43)	27.5	8/26 (30.77)	14/26 (53.85)	4/26 (15.38)
Hb E disease	12 (1.02)	9	3/11 (27.27)	3/11 (27.27)	5/11 (45.45)
Hb-E trait	14 (1.19)	26	2/8 (25)	3/8 (37.50)	3/8 (37.50)
Others (H, Punjab D etc.)	5 (0.42)	4	5/5 (100)	0/5 (0)	0/5 (0)
Total	1178		712/1063 (66.98)	259/1063 (24.36)	72/1063 (8.66)

Figure: Pattern of Thalassemia and transfusion practices in Bangladesh. (Hossain M. S., Raheem. E., Sultana. T. A., Ferdous. S., et al., May 2017)

Iron chelation and hydroxyurea therapy

In a study, approximately 43% of the patients (n = 972) with multiple blood transfusions were treated with iron chelators to remove excess iron from the body. Deferiprone was the most commonly used iron chelator (n = 481) followed by Deferasirox (n = 199) and Desferal (n = 91). Hydroxyurea therapy was given to nearly 43% of the patients (n = 972) who underwent transfusions regularly or occasionally to increase fetal hemoglobin and reduce ineffective erythropoiesis (Hossain M.S., Raheem E., Sultana T.A. et al., 2017)

Treatment cost of thalassemia in Bangladesh:

The expense of treatment differs based on age, body weight and severity of the thalassemia disease. The most conservative direct medical cost ranges from BDT 127,000 (USD 1632; USD 1 = BDT 78) to BDT 309,000 (USD 3960) per year. In Bangladesh, there is no national insurance system or any sponsored or free treatment system from the government health facilities. It is predicted that patients must provide all the treatment cost and it is too difficult for most of the families to manage to pay for proper treatment. More than 72% of the patients (n = 448) monthly household earning was between BDT 10,000 (USD 128) to BDT 20,000 (USD 256), signifying a massive economic problem that could render seeking treatment for most thalassemia patients impracticable in Bangladesh (Hossain M.S., Raheem E. et al., 2017)

Table 2 Conservative estimate of treatment cost at Thalassemia Foundation Hospital, Bangladesh

Requirements	Cost (USD)		
	1–10 years	11–20 years	21–30 years
Blood Transfusion plus filter/month	32 (1 unit)	65 (2 units)	96 (3 units)
Iron chelation (Desferrioxamine/deferasirox)	65 (25 vials)	130 (50 vials)	195 (75 vials)
Hospital care 1 day/month	26	26	26
Lab tests/month	13	13	13
Total cost/month	136	234	330
Total cost/year	1632	2808	3960

(Hossain S. M., Raheem. E., Sultana. T. A., Ferdous. S., et al., 2017)

Recommendations for the younger generation in Bangladesh:

Thalassemia creates a noteworthy burden on healthcare systems in endemic regions since the lifetime management charge of thalassemia is beyond the capability of resource-constrained countries. It is predicted that only 12% of patients with transfusion-dependent thalassemia are appropriately transfused and of those, less than 40% have access to satisfactory iron chelation (Modell B., Darlison M., et al., 2008). Due to augmented life expectancy and slowing population growth, Bangladesh is now going through the double burden of communicable and non-communicable diseases (NCDs) (Islam A., Biswas T., et al., 2014). At present in Bangladesh, non-communicable diseases are responsible for 59% of total deaths which in turn has created a strain on the present healthcare system in the country. The government of Bangladesh spends only US $26.60 per capita for healthcare services (Ahmed SM, Alam BB, Anwar I, Begum T, Khan JA, Nababan H, et al., 2015). The management of the disease is complicated and expensive. There is no cure for thalassemia except for allogeneic BMT in a chosen group of patients which again is a very costly treatment option. The management of this disease is also very costly. As referred previously, an average Bangladeshi family has to disburse more than their monthly household income for a thalassemia major patient. However, the prevention of thalassemia is cost-effective; at least four times less expensive than treating thalassemia based on a study conducted in Israel (Koren A, Profeta L, Palmor H, Levin C, Zamir RB, et al., 2014). There is a saying that prevention is better than cure. Prevention is therefore likely to be the most viable tactic to decrease the economic burden of the thalassemia patients on families and to generate a sustainable healthcare system.

Pre-marital screening

Pre-marital screening is defined as a test in which couples that are going to get married are tested for genetic, infectious and blood transmitted diseases to prevent any risk of transmitting any disease to their children. Nowadays premarital testing is considered an important issue, as a result of the increase in the number of children affected with genetic or blood transmitted diseases. Genetic counseling is an important part of pre-marital screening. In our country, maximum people are unaware of the growing concern regarding thalassemia. Genetic counselors can help to decide the type of test the couple should consider. A detail of the family history, medical records, and conditions of family members from both sides needs to be provided to the counselors to have proper advice from him.

If the couple is informed of the possibility that they are at an increased risk of having a genetically abnormal child, they can choose to plan conceptions according to medical advice and can make use of the genetic counseling services available, such as:

- Couples may choose not to get married
- If couples agree to get married, they may not decide to have children
- If couples decide to have children, they must do the pre-marital screening of the fetus at an early stage of pregnancy
- The pair must recognize the option of termination of the pregnancy
- The pair must realize the social, economic perspectives of having children with genetic disorders.

(Swack N., et al, 1988).

A primary preventive program is relied on the carrier [heterozygous] detection and counseling to discourage marriage between thalassemia trait (carriers). Allover, premarital screening for thalassemia and other preventable genetic diseases are wide-ranging in many parts of the world. The achievement of mandatory premarital screening with genetic counseling was only effective in reducing β-thalassemia births in some Middle Eastern countries (Iran, Turkey) because of widespread consciousness, screening timing and accessibility to prenatal diagnosis (PND) and the choice of therapeutic abortion (Saffi M, Howard N, 2015). Along with that, Taiwan decided to adopt a national screening program in 1993 to minimize the blowout of thalassemia which appreciated considerable success, with less than three per year of thalassemia births in last 10 years (Peng CT, Liu SC, Peng YC, et al.; 2013). Prevention through pre-marital and genetic screening is uncertainly the best approach to forestall thalassemia considering socio-religious matters among other aspects. In conservative societies likely in Bangladesh, marriage issue has become a very complex social phenomenon where couples are typically chosen based on solid personal preference as well as traditional reasons. Based on the thalassemia carrier status, if a prearranged marriage is backed out, it may be able to create social embarrassment or stigmatization for the young couples and their families.

Goals of Premarital Screening Program:

- Restraining the spread of some genetic blood diseases (e.g. sickle-cell anemia and thalassemia) and infectious diseases (e.g. hepatitis B, hepatitis C, and HIV/AIDS).
- Promoting alertness about the notion of a comprehensive healthy marriage.
- Reducing pressure from the health institutions and blood banks in Bangladesh.
- Dodging the social and psychological complications for the families whose children suffer from such genetic disorders.
- Lessening the family and society's economic barriers to treat diseased persons.

(Swack N., et al, 1988).

Figure: Genetic Counseling

Target Screening Approaches

Since there are insufficient healthcare access as well as infrastructure and financial limitations in Bangladesh, the antenatal screening in pregnant women is not a practically feasible approach since the vast majority of the women, specifically in resource-limited rural areas, cannot be screened. Under these situations, a selective screening approach within the families suffering from thalassemia could be a feasible approach in Bangladesh. In the study, anecdotal data (n = 605) on the family background of thalassemia acclaim that 20% had another thalassemic siblings while 3% had two or more siblings with thalassemia. Most of the thalassemic couples in Bangladesh are selected retrospectively after the diagnosis of one or more affected children: this could be used as a stand-in indicator to test extended family to craft an effective carrier identification method in Bangladesh. If the respected authorities can spread the public health-related messages throughout the country appropriately to the affected and extended families, this could promote consciousness of genetic susceptibility to thalassemia. In Sardinia, this procedure was applied to only 15% of the mature populace which led to the diagnosis of 90% of predicted vulnerable couples (Saffi M, Howard N., 2015).

Prenatal screening

A secondary prevention strategy emphasizes on prenatal diagnosis followed by genetic counseling for the termination of pregnancy. The acceptability of the prenatal diagnosis and selective termination/abortion of an affected fetus is determined by various factors including religious, social and cultural upbringings, personal experiences and beliefs. Henceforth, ethical guidelines concerning genetic counseling, carrier screening, and prenatal diagnosis must be evaluated in the context of each society or country. Bangladesh is mainly a Muslim majority country and social practices are heavily influenced by religious ideologies. From the viewpoint of Islamic jurisprudence, it is acceptable to perform an abortion to protect a mother’s life or health, or because of fetal anomaly which is unsuited with life (Al-Matary A, Ali J., 2014). A research operated in the highly conservative Muslim society of Pakistan has publicized that selective termination is acknowledged by affected parents irrespective of religious and social groups after genetic counseling (Ahmed S, Saleem M, Sultana N, Raashid Y, Waqar A, Anwar M, et al., 2000). Since abortion has become a highly sensitive issue from an Islamic religious standpoint, faults are not acceptable in the diagnosis of fetal anomalies (Al-Matary A, Ali J., 2014).

Necessity of Thalassemia Prevention Program in Bangladesh:

In a third world country like Bangladesh, a comprehensive thalassemia prevention program has become an urgent need of the time. This kind of program is cost-efficient as well. It has been noticed that allover expense per case prevented was lower than the expense of a single year of treatment for a particular individual. Examples of neighboring countries present an improving graph of acceptance regarding preventative strategies against thalassemia. To note that in Sri Lanka "safe marriage concept" shaped the basis of the National Thalassemia Prevention Program since selective abortion is illegitimate as well as unacceptable on religious backgrounds. Premarital screening was believed to meet with acceptance because of it's being akin to comparison of horoscopes to assess compatibility, a cultural exercise extensively undertaken preceding to wedding in Sri Lanka (Mudiyanse RM, et al., 2006). Countries that have attained success with the prevention of thalassemia have provided genetic counseling on the importance of getting tested, persuasion at the individual level and guidance on the interpretation of test results. It is recommended to integrate thalassemia prevention in the school curriculum. Public consciousness programs should be arranged through print and electronic media which are complemented by more thorough education and counseling programs delivered through public health field staff, general practitioners and outpatient departments of the government hospitals. Making screening obligatory is a policy that may need serious consideration if screening rates remain low even after these facilities are in place. As per this survey, 77% were in agreement with mandatory screening. According to a similar survey in Pakistan, 95% of parents and 90% of doctors have decided to go to genetic counseling (Cousens NE, Gaff CL, Daltycki MB, 2010). A previous public survey in Sri Lanka has documented 96% of people agreed that at least one person in a couple should undergo screening (Cousens NE, Gaff CL, Daltycki MB, 2010).

Thalassemia has been encroaching into the south-east Asian region for the last decades. Since our neighboring countries are speeding up its resistance towards thalassemia and shaping its defense, we have to urgently be ready to set up our plan to take on a comprehensive thalassemia prevention program to encounter thalassemia disease in our country. Virtually, we have no information on the true burden, genetic spectrum, clinical outcome, morbidity and mortality due to thalassemia in Bangladesh. This is why research is the most important priority to establish thalassemia as one of the major public health issues of Bangladesh. The creation of better-quality diagnostics and treatment services for thalassemia notably in a one-stop center is an important achievement towards thalassemia prevention. Health ministry should arrange educational and counseling programs not only in urban areas but also in the remote corners of our country. Print and electronic media should take the initiative of spreading the thalassemia across the country. Religious hurdle is also an issue in this case. So, respected religious scholars should be included in the prevention policy in our country. Private-public partnerships should be strengthened in this regard to ease the tension regarding thalassemia disorder.

Conclusion:

The current observation shows us that almost all over treatment tactics are predominant in Bangladesh. We observed a significant percentage of beta-thalassemia carriers receiving blood transfusion. As stated earlier, it could have been because of misdiagnosis (e.g. concurrent iron/ vitamin deficiency) or a higher target Hb level for the thalassemia patients due to lack of alertness among the practicing physicians. Beta-thalassemia carriers (trait) may have mild anemia with Hb level starting from 9 to 12 g/dL. This level does not ensure transfusion to standardize the Hb level. Individual response and adaptation to anemia may also play an important role in selecting patients for transfusion. On the other hand, in the case of HbE beta-thalassemia, the most critical issue is to determine transfusion dependence. Other neighboring countries like Sri Lanka may be presented as a role model to re-evaluate the transfusion practices in Bangladesh, as regards to thalassemia (Olivieri NF, Muraca GM, O'Donnell A, 2008). Modification of the existing candidate selection criteria for transfusion requirement, which is mostly based on Hb level currently practice in Bangladesh, will play a significant role in screening outpatients that might benefit from other essential yet often neglected therapeutic interventions. Further investigations are required to understand the epidemiology, mutation spectrum, clinical course and treatment outcomes in this thalassemia prone country, which is undergoing demographic transition.

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