Lec 8: Thalassemia

1. Definition: Thalassemia is a hereditary blood disorder characterized by reduced or absent synthesis of A or B-globin chains, leading to defective hemoglobin production, microcytic hypochromic anemia, and varying clinical severity.

2. Genetic Basis

1. Inherited in an autosomal recessive pattern.
2. Alpha-thalassemia results from deletions/mutations of one or more a-globin genes (normally four genes present).
3. Beta-thalassemia results from point mutations affecting transcription, RNA processing, or translation of the b-globin gene.

Types of Thalassemia

A. Alpha Thalassemia

• One gene deletion: Silent carrier, asymptomatic.

• Two gene deletions: a-thalassemia trait, mild anemia.

• Three gene deletions: HbH disease (bn), hemolytic anemia, splenomegaly.

• Four gene deletions: Hydrops fetalis (Hb Bart's, gn), incompatible with life.

B. Beta Thalassemia

- Minor type (B+)when mutation caused deletion of one beta chain،
- Major β (B–) Thalassemia called (Cooley's Anemia) that defect in both beta chains (the towbeta chains are absent).

A. Minor: Mild microcytic anemia, elevated HbA2.
B. Intermedia: Moderate anemia, may require occasional transfusions.
C. Major: Severe anemia, transfusion-dependent, presents at 6–12 months of age.

4. Pathophysiology

• Imbalanced globin chain production leads to precipitation of unpaired chains.

• This causes RBC membrane damage, ineffective erythropoiesis, and extravascular hemolysis.

• Bone marrow expansion leads to skeletal deformities (frontal bossing, maxillary enlargement).

• Increased iron absorption and repeated transfusions lead to iron overload and organ damage.

5. Clinical Features

1. Mild forms: Often asymptomatic or mild anemia.
2. Severe forms:

- Growth retardation, failure to thrive.
- Jaundice, splenomegaly, hepatomegaly.
- Bone deformities ("crew-cut skull").
- Iron overload causing cardiomyopathy, endocrine failure, liver cirrhosis.

6. Laboratory Findings

1. CBC: Microcytic hypochromic anemia, low MCV.
2. Peripheral smear: Target cells, anisopoikilocytosis, basophilic stippling.
3. Electrophoresis:

- B-minor(B+): -HbA2, ±-HbF.
- B-major(B-) : -HbF, ¯/absent HbA.

4. Iron studies: Normal or high ferritin.

5. Genetic testing: confirms diagnosis.

7. Differential Diagnosis

1. Iron deficiency anemia.
2. Sideroblastic anemia.
3. Anemia of chronic disease.
4. Lead poisoning.

8. Complications

1. Iron overload lead to cardiac failure, liver cirrhosis, diabetes, endocrine dysfunction.
2. Hypersplenism.
3. Infection risk, especially post-splenectomy.

9. Management

Beta-thalassemia major:

1. Regular transfusions (maintain Hb > 9–10 g/dL).
2. Iron chelation (deferoxamine, deferiprone, deferasirox).
3. Folic acid supplementation.
4. Splenectomy if transfusion requirement increases.
5. Bone marrow transplantation (curative in selected cases).

Alpha-thalassemia (HbH disease):

1. Folic acid.
2. Avoid oxidative drugs/infections.
3. Transfusions when needed.

10. Prevention

1. Carrier detection programs.
2. Premarital screening.
3. Prenatal diagnosis using CVS or amniocentesis.