Thalassaemia

By
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Definition

- Group of hereditary disorders characterized by a genetic deficiency in the synthesis of alpha or beta-globin chains

Historical background
Beta thalassemia

- First described by Cooley and Lee in 1925.
- Mediteranian ancestry.
  - Cooley's Anemia
  - Mediteranian Anemia

Review of hemoglobin structure

- In the adult ……three hemoglobin types
  - Hgb A…. 2 alpha & 2 beta chains - 95% of total
  - Hgb A2… 2 alpha & 2 delta chains - 3% of total
  - Hgb F… 2 alpha & 2 gamma chains - 2% of total

Geografical Distribution

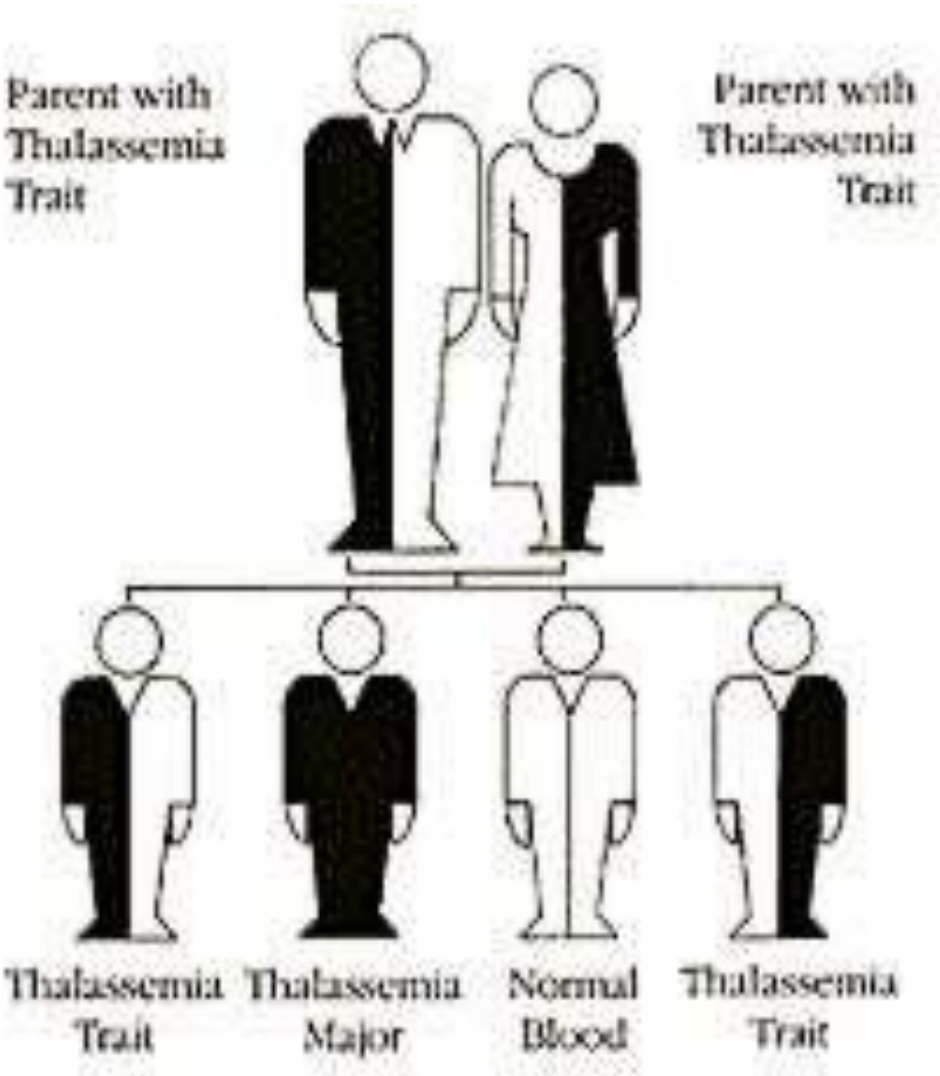
- Mediterranean Italians
- Greeks,
- Arabian Peninsula, Iran, Africa, Southeast Asia southern China.

Indian/Pakistani origin

- b-thalassemia trait
  - 1-15%
- α-thalassemia
  - 5–10%
- Hemoglobin D trait
  - 1-3%

Genetics

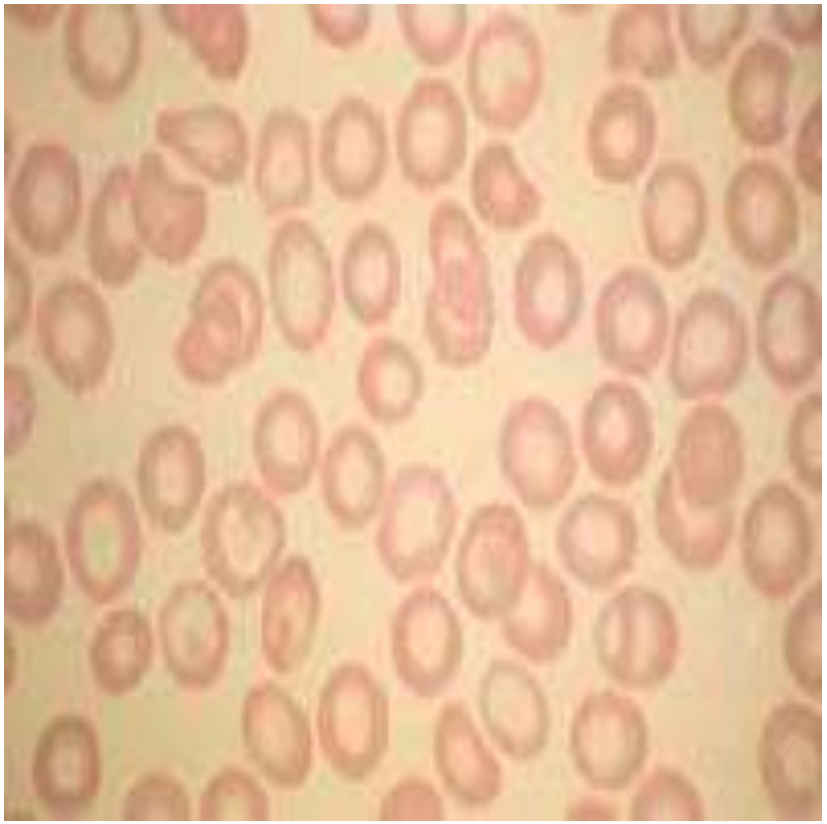
- Autosomal Recessive

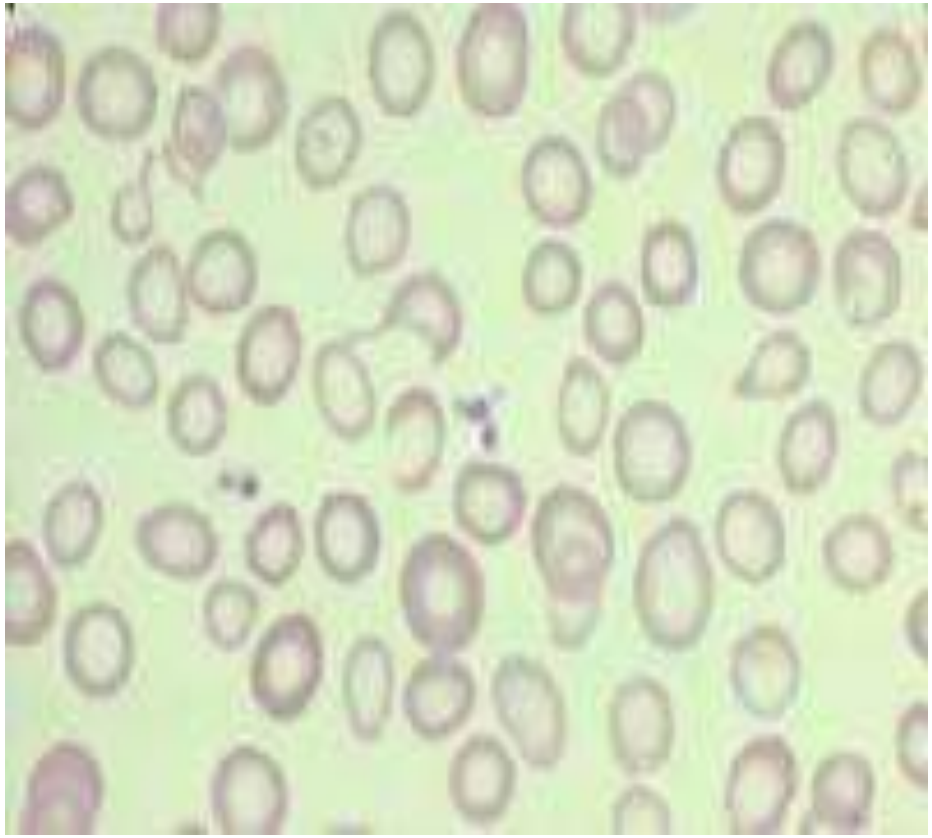


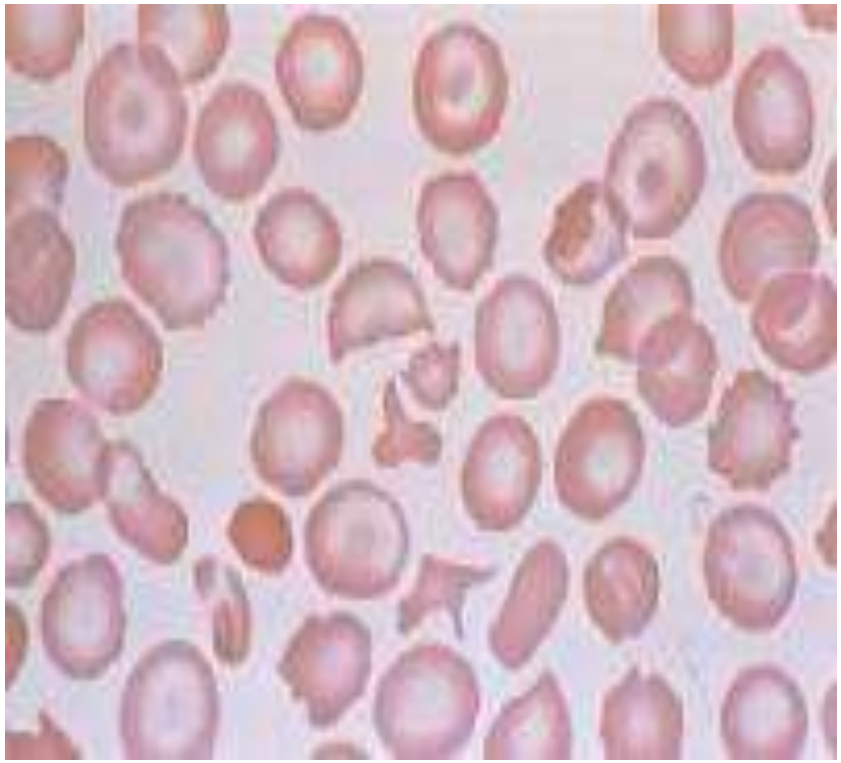
Pathophysiology:

- Imbalance between the normal rate of alpha-chain production and the impaired rate of beta-chain production.
- Beta+ thalassemia
  - Decreased beta-chain production
- Beta -0 thalassemia
  - Absent beta-chain production.

- less hemoglobin deposited in each RBC…. hypochromasia.
- The Hb deficiency …….microcytosis.
- In Silent carrier state both Hb level and RBC indices remain normal.







Elevated A2 Hb

- delta chains that, by pairing with the alpha chains, produce Hb A2 (about 2.5-3% of the total Hb).
- due to the increased utilization of delta chains by the excessive free alpha chains
- The delta gene has physiological limitation in its ability to produce adequate delta chains

Hemolysis in thalassemia

- The remaining alpha chains precipitate in the cells → reacting with cell membranes → intervening with normal cell division acting as foreign bodies → destruction of RBCs.
- Ineffective erythropoiesis
- Erythroid hyperplasia and extramedullary hematopoiesis.

TYPES OF BETA THALASSEMIA

1-Hetrozygous States

Thalassemia Minor

2-Homozygous States

Thalassemia Intermedia

Thalassemia Major

Clinical feature
Thalassemia Major

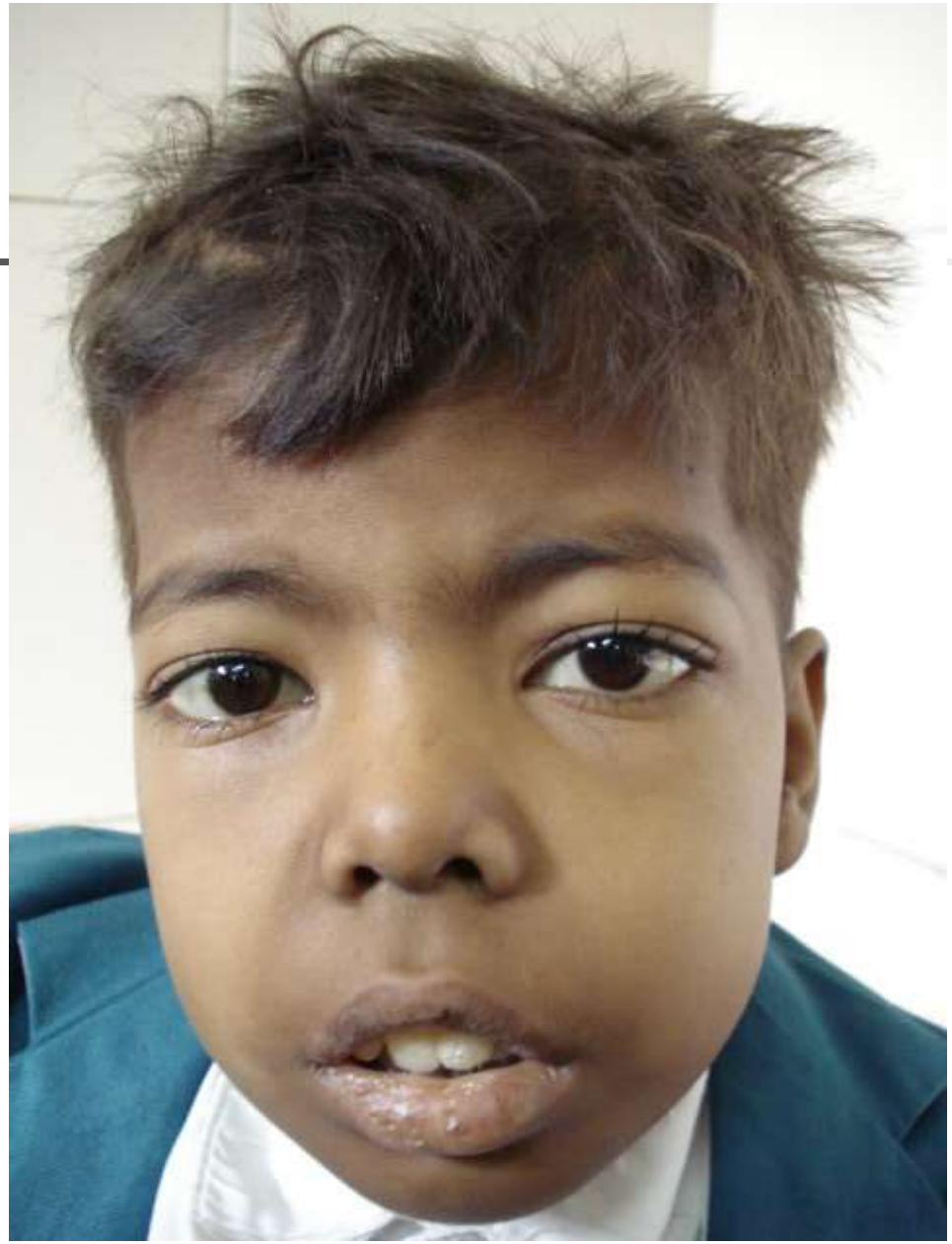
- Age of presentation
  - 6-12 months of life
- Fatigue, poor appetite, and lethargy
- Abdominal distention
- Failure to gain weight
- History of consanguinity
- Similar history in family

Systemic review

- Polyuria & polydipsia
- Jaundice
- Constipation, lethargy
- Breathlessness on exertion, edema
- Tetany, fits

Examination

- Pallor
- Jaundice
- Height & weight
- Greenish yellow hue pigmentation
- Typical facies (maxillary hyperplasia, flat nasal bridge, frontal bossing
- Hepatosplenomegaly



Thalassemia Minor

- asymptomatic mild microcytic anemia
- Detected through routine blood tests

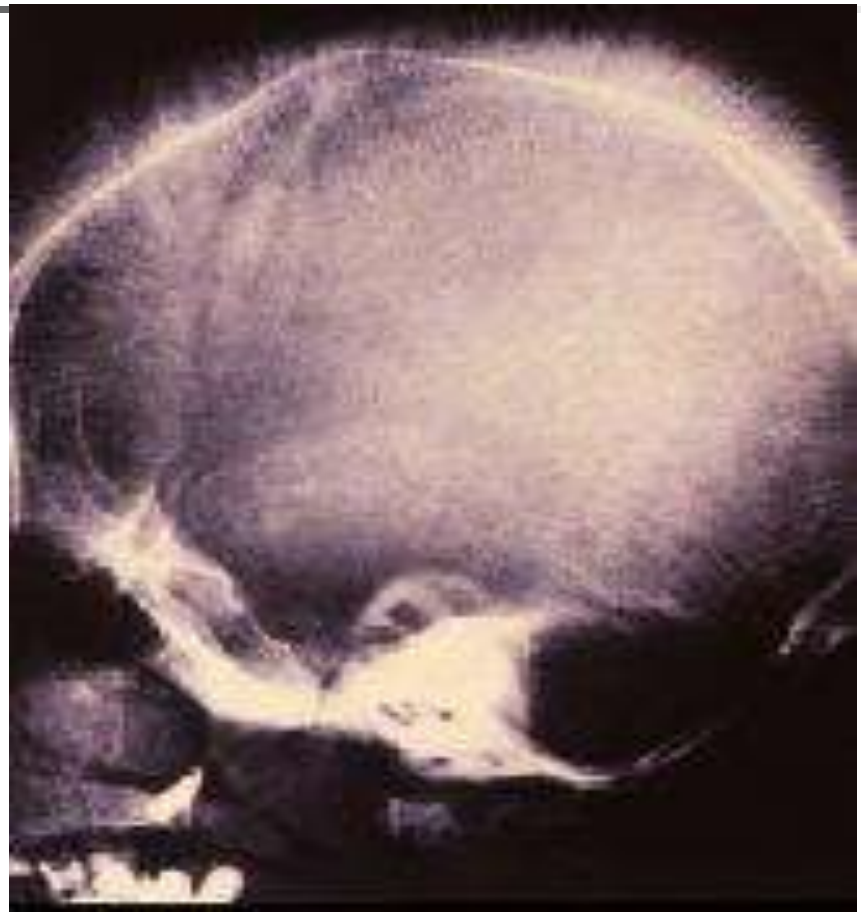
Investigations

- Blood count, ESR, RBC morphology & Retic Count
- Hb Electrophoresis
- Serum Ferritin
- Chest X-Rays

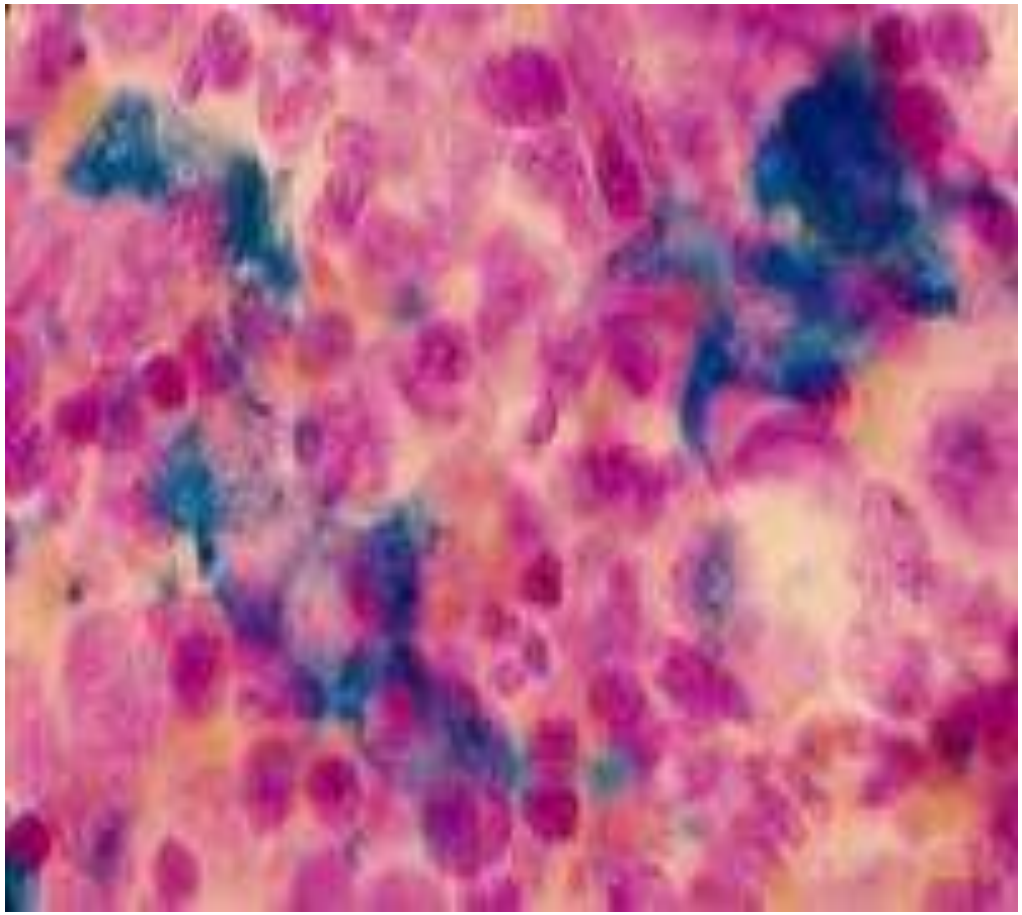
Hemoglobin Electrophoresis

- Thalassemia Minor
  - Decreased HbA1
  - Elevated HbA2 upto 10% (normal 2.5%)
  - Elevated HbF upto 7% (normal <2.0%)
- Thalassemia Intermedia
  - Decreased HbA1 (20-40%)
  - HbA2 always elevated
  - HbF is 60-80% of total hemoglobin
- Thalassemia Major
  - Absent AbA1
  - Elevated HbA2 (>3%)
  - HbF (>90% HbF may be 100%at birth)

Skull X-Rays



Bone Marrow Aspiration



Management

- General
  - Counselling of parents
  - Diet
  - Tab folic acid
  - Vitamin C
  - Vaccination
    - Hepatitis B

Specific

- Regular blood transfusion
  - Keep Hb upto 10 gm%
- Super blood transfusion
  - Keep Hb upto 12 gm%
- Packed cells transfusion
  - Three or four weekly
    - 15 to 20 ml/kg

Chelation Therapy

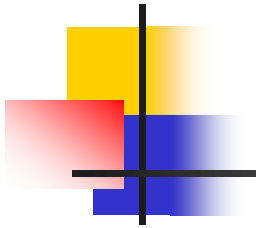
- Desferoxamine
  - 20-60 mg/kg Subcutaneously over 8-12 hrs
  - 5-6 night /week
- Defriperone
  - Oral chelator
  - Alone has poor response and severe side effects
- Asunra
  - Expensive with good response

Other modalities

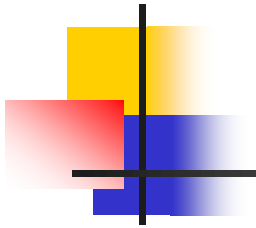
- Splenectomy
  - Hypersplenisim
  - Increased blood transfusion requirement
  - Large Spleen
- Bone Marrow Transplantation
  - Definitive

Complications

- Congestive heart failure
  - Severe aneamia
  - Cardiomyopathy
- Transfusion reactions
  - Acute
  - Late
- Blood borne infections



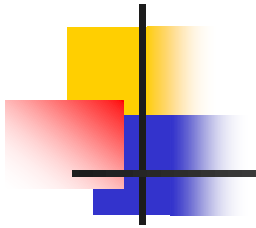
- Hemosidrosis
  - Endocrinopathy
    - Diabetes mellitus
    - Hypoparathyroidism
    - Hypothyroidism
    - Hypogonadism
- Chronic liver disease



- Side effect of chelation therapy
  - Retinopathy
  - Deafness
  - Metabolic bone disease
  - Agranulocytosis

PROGNOSIS

- Increase quality of life with proper management
- Death due to congestive heart failure is common
- Bone marrow transplantation is curative



Thankyou