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Clinical Review of Thalassemia: Kinds, Signs Management, and Globin Structure

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Summary: Thalassemia is a blood disease in which the typical hemoglobin is synthesized in minor quantities than normal. It is genetic disease consequently it passed from parents via their genes. Thalassemia patients cannot synthesize sufficient typical hemoglobin, that causes serious anemia. Hemoglobin is present in erythrocytes and transports O2 to all organs of the body. Around the world, there are approximately 30 million carriers in addition to about 10000 babies have thalassemia annually. In fact, two main types of thalassemia are found. These types are Alpha thalassemia which affected by Alpha globin gene and Beta Thalassemia which affected by Beta globin gene. In this review we focus on thalassemia disorder, kinds and its management.

Keywords: Thalassemia, hemoglobin, Anemia, Alpha thalassemia, Beta Thalassemia , Blood transfusions.

Introduction

Thalassemia " also called Mediterranean anemia" derived from the Greek word “Thalassa” which means sea, and “emia” which means blood [1,2]. Specially in the developing states, thalassemia is considered as an enormous health problem [3].

It was discovered in 1925 in Italian kids with early childhood mortality, acute anemia, and enlargement in abdominal organs. Thalassemia is caused by an abnormal structure of hemoglobin. Thus the body destroys erythrocytes, leading to anemia. So, the body produces further erythrocytes more rapidly, causing many complications for instance enlargement of spleen, bone deficiency and heart disease. Generally, thalassemia is single-gene disease, which caused by a set of hereditary disorders with reduced or lacking β-globin chain production, resulting in a decreasing of hemoglobulin (Hb) in red blood cells (RBCs) in which the level of Hb is less than normal [4].

This disease is resulted from the defect in production of globin chain in the hemoglobin (made up of 4 polypeptide chains), causing considerably less O2 attached to the hemoglobin and transfer throughout the body. Thalassemia is classified α, β, γ and δ according to which polypeptide chain is defected, β-thalassemia is occur when the β chain is defected [1,5].

Beta-thalassemia:

Beta-thalassemia occurs by a deficiency in two β-type chains [6], consisting of Hb and classified into:

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1. **Thalassemia minor:** which considered as heterozygous type in which about 20% of polypeptide production is reduced. This reduction is compensate by production of extra HbA2. It caused by a single chain disorder, the patient is asymptomatic, and displays a simple anemia [7].
2. **Intermediate thalassemia:** it is a transitional state between minor and major forms, in which patients can live a normal life, however require infrequent blood during disease [7].
3. **Thalassemia major**: which is a homozygous type hence both alleles are mutated thus β chain production is completely blocked. This reduction is compensate by production of extra HbF. Hence patients have serious anemia, so they require frequent blood transfusions for normal living, the signs do not happen at the birth, but in the first two years of the kid's life [7].

Alpha thalassemia

All human diploid cells have 4 copies of alphaglobin gene [8]. The α-thalassemia is caused by the decrease of the production of the α-globin chains [9,10]. There are 2 main kinds of α-thalassemia which are: hemoglobin H disease which is milder than β-thalassemia and is not commonly need blood transfusion treatment and α-thalassemia major which is a very severe anemia which may arises before birth. Most infected children do not may die after birth. [11].

It was found that > 200 various mutations may lead to the ß-globin gene, founding on the chromosome 11. Different ß-chain dysfunction mutations may occur in various ways [12,13]. Molecular DNA techniques which examine the mutations in thalassemia patients help prediction of infection strictness, especially in fetus in the earlier pregnancy stages (Prenatal analysis) [14, 15].

Symptoms of Thalassemia

1- **Iron overload:** It is the main complications affected to patients with regular blood transfusion resulting in damage of liver and heart.
2- **Bones defect**: the normal body growth is affected. Therefore, the patient has skeletal malformations, additionally, the face bones and the skull will be thicker.
3- **spleen Enlargement**: it resulted from viral or bacterial agents, liver failures as well as the contaminated blood.
4- **Other symptoms:** For instance, Fatigue, Dark urine, breath Shortness and pale skin. [11]

Treatment of Thalassemia

The principal technique of thalassemia treatment is the blood transfusion [3]. Blood transfusion resulting in accumulation of increased quantities of iron in the body which cannot be eliminated naturally. Consequently, this is the main reason of mortality in most thalassemia patients. Later, a drug called deferoxamine was discovered to eliminate the excess iron that accumulated in the body. deferoxamine prevents iron-inducted heart problems. Newly, two oral medications have supported the patient's life with iron overload from transfusions for thalassemia [14].

Iron-chelating agents must be used appropriately; if not, recurrent blood transfusion may resulting in iron overload. However, without blood transfusions, the increased level of erythropoiesis improve nutritional iron absorption by the gut, causing intense overload [15]. which

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may resulting in severe destruction to different organs, such as, by the deposition of iron in heart, liver. Cardiotoxicity is considered as the greatest serious complication of iron accumulation, that requires chelation treatment [15, 16].

Thalassemia Management

High iron levels regularly accumulated in the body of thalassemia patients. This accumulation cause various biochemical complications. Ferritin and transferrin are substances involving in iron transportation and storage. Ferritin is protein found in the cell which attach to Fe(II) and stores it in Fe(III) form, while Transferrin is iron-binding protein found in plasma and transport iron in the blood [17]. Thalassemia treatment based on the severity. In mild type of thalassemia, recommendation and psychotherapy are necessary. While for more severe type of thalassemia, management might include blood transfusion; by iron-chelating agents drugs for example deferiprone, deferoxamine, or deferasirox to avoid the hemoglobin breakdown, or by using bone marrow [18].

Regular Structure and Gene Clusters Expression of Globin

Hemoglobin of human is considered as a heterotetramer protein, consist of 2 α and 2 β subunits (Figure 1). All subunits have a heme groups, that is iron containing complex which attach to O2 [19,20]. The production of hemoglobin is maintained via two developmentally controlled multigene cluster: the α-like globin cluster in chromosome-16 and the β-like 9.5 chromosome 11. In the normal people, the production of α and β globin chain is balanced finely through the terminal erythroid differentiation however the way of balanced expression is still unknown [20,21,22].

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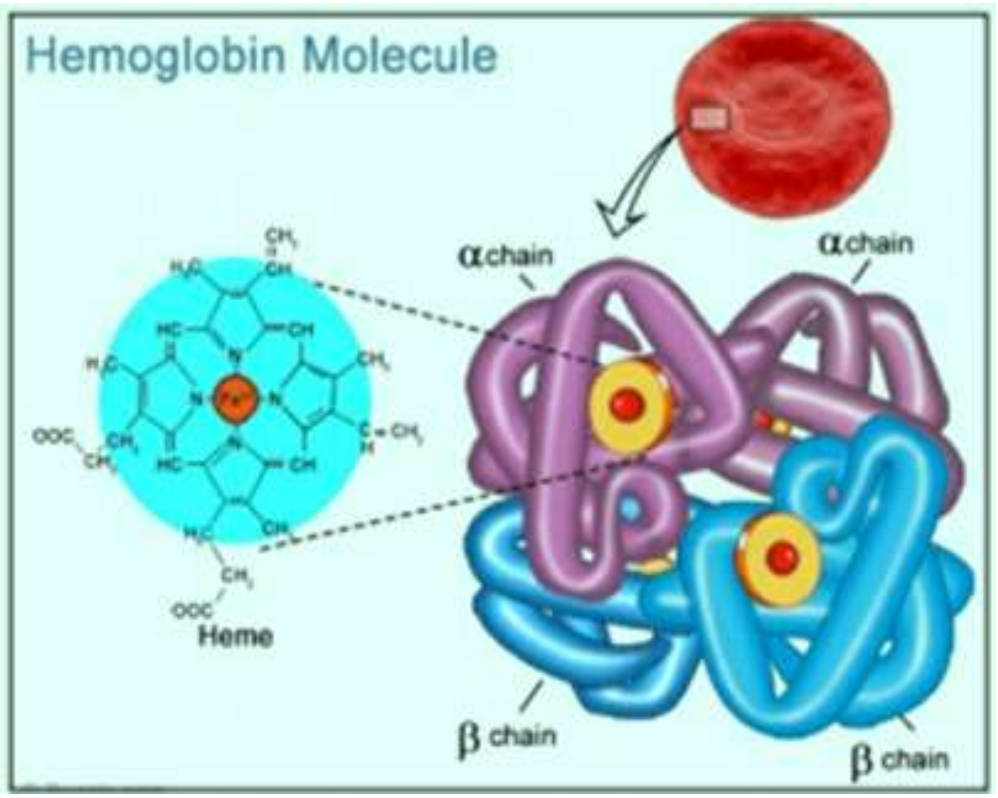

Figure 1: structure of hemoglobin.

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