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Original Articles

Psychological Aspects of Thalassemia Disease

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Abstract:

Hemoglobin is a protein present in erythrocytes responsible for carrying oxygen throughout the body. A hemoglobin molecule has two sub-units usually indicated to as alpha and beta. Both sub-units are necessary to bind oxygen and deliver it to cells and tissues in the body. The gene that controlled the production of alpha chains is called the alpha globin gene cluster, and similarly the beta globin gene produced beta chains. Thalassemia is characterized as hemoglobinopathy, which means that it is pathophysiology that which occurs due to hemoglobin protein deficiency found in red blood cells (RBCS). More specifically, alpha and beta thalassemia are caused by gene mutations that code for the alpha and beta globin chains that make up the quaternary structure of hemoglobin. Thalassemia is a genetic disorder with mutations in the a-globin (chromosome 16) or B-globin (chromosome 11) gene, resulting in a loss of the affected globin chain but an accumulation of the non-affected one, resulting in an excess in the globin chain. As a consequence, inadequate erythropoiesis, damage to erythroid membranes and spleen obstruction may occur.The term "thalassemia" derives from Greek words (Thalassa) meaning sea and blood (Heam)The two major types of thalassemia, alpha and beta, are named after defects in these protein chains. Severe forms usually are diagnosed in early childhood and are lifelong conditions.

Keywords: Thalassemia, Disease, Hemoglobin, Psychology

Introduction:

The hemoglobinopathies refer to a diverse group of inherited disorders characterized by a reduced synthesis of one or more globin chains (thalassemia) or the synthesis of structurally abnormal hemoglobin (HbS) (Saleh-Gohari & Mohammadi-Anaie, 2012). Thalassemia is one of the world's most frequent hereditary illnesses. It's a severe health issue that causes a lot of morbidities, early mortality, and a lot of financial and emotional hardship for a family (Al-badry & Al- tamemi, 2019). Thalassemia has known as a genetic defect that is autosomal recessive, characterized by a reduction or absence of production one and/or two types of globin chains. This condition will have an impact on the quantity and quality of blood produced (Husna et al., 2017). Thalassemia is also

a genetic disorder condition characterized by an abnormal form of hemoglobin production by the body. Depending on which kind of globin is mutated, there have been two forms of thalassemia, alpha-thalassemia and beta-thalassemia. When one or more from the four a-globin genes are destroyed altered, or a-thalassemia occurs, while B-thalassemia evolves when both B-globin genes are damaged or mutated. Furthermore, thalassemia major occurs when a child receives two defective globin genes, one from any parents, whereas thalassemia minor occurs when a child receives just one deficient globin gene (Abu-Shaheen al., 2020). et Thalassemia is derived from the Greek word that taken from two words, Thalassa meaning the Sea and Emia means blood, thus called Mediterranean anemia or Cooley's anemia. Thalassemia is a congenital hemolytic disease that inherited according to Mendel's laws, The first an American scientist named Dr. Cooley defined it's to other in1925. Thalassemia syndromes most common recessives diseases worldwide, with an estimation of 1-5% of the global population carriers of a genetic thalassemia mutation (Rund & Rachmilewitz, 2005). They are predominant in countries around the Mediterranean, the Middle East, and parts of Central Asia, southern China, India and the northern states. The marriage and immigrant populations between different ethnic groups causes thalassemia to be common between all countries, the majority of them are in developing countries (Vichinsky, 2005).

Aim of the study

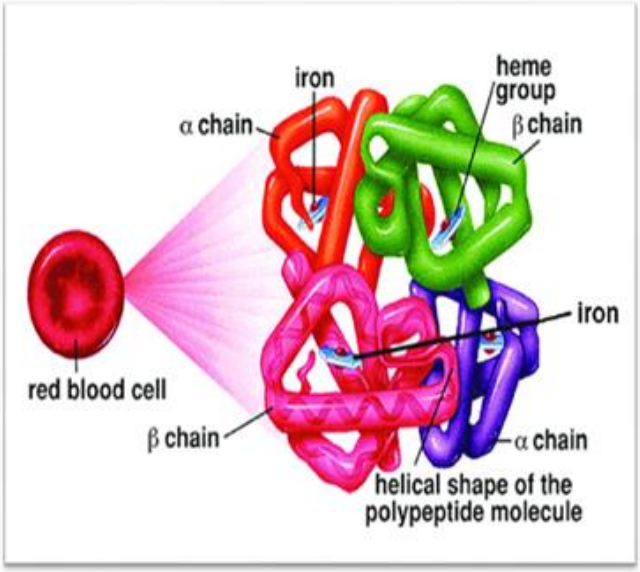
The objectives of this study were to determine the _ physiological aspects on thalassemia and Study of modern technologies used in diagnosing and treating disease and how to prevent it.

Hemoglobin

is the vital protein that conveys oxygen from the lungs to the tissues and facilitates the return of carbon dioxide from the tissues back to the lungs. Like all proteins, it is made of the small organic molecules called amino acids, strung together in a linear sequence called a polypeptide chain. The amino acids are of 20 different kinds and their sequence in the chain is genetically de- termined. (Li, 2017).

The normal structure of hemoglobin

A hemoglobin molecule is made up of four polypeptide chains, two alpha chains of 141 amino acid residues each and two beta chains of 146 residues each. The alpha and beta chains have different sequences of amino acids but fold up to form similar three-dimen- sional structures. Each chain harbors one heme, which gives blood its red color. The heme consists of a ring of carbon, nitrogen and hydrogen atoms called porphyrin, with an atom of iron, like a jewel, at its center. , which includes, in addition to iron, the tetracyclic pyrrole ring, which consists of succinic acid and glycine thanks to the enzyme .8-amino laevulinic acid dehydrase. Hemoglobin iron constitutes two-thirds of the body's iron, while the rest is iron ready for metabolism. A single poly- peptide chain combined with a single heme is called a subunit of hemoglobin or a monomer of tthe molecule. In the complete molecule four subunits are closely joined to form a tetramer (Daraghmeh, 2016).



Figer 1. Structure of Hemoglobin
(Hemoglobin.gen.tr, https:// hemoglobin.gen.tr/, Access date: 13.02.2021)

(Haemoglobin A) in adults, which is afour-dimensional(tetramer) consists of two alpha chains and two beta chains (Alfa2 and Beta2) and constitutes 97%, while small amounts of fetal hemoglobin (HbF) are composed of two gamma chains and two alpha chains (Gama2 and ALFA2) in the form of The percentage is less than 1%, but in the type HBA2, which consists of two alpha and

two delta chains (delta2, Alfa2), it constitutes a percentage of (2.5%) (Hoffman et al., 2013).

unction of Hemoglobin in the Human Body

Hemoglobin is an oxygen carrier

The major function of hemoglobin is the transportation of oxygen from lungs to all the tissues of the body. The oxygen binding capacity of hemoglobin is 1.34 mL 02 per gram. Each globin subunit of the hemoglobin molecule can bind with one Fe2+ ion. The affinity of hemoglobin towards oxygen is gained by the Fe2+ ion. Each Fe2+ can bind with one oxygen molecule. The binding of oxygen oxidizes Fe2+ into Fe3+. One atom of the oxygen molecule, which binds to Fe2+ becomes a superoxide, where the other oxygen atom protrudes at an angle. The oxygen-bound hemoglobin is referred to as oxyhemoglobin. When blood reaches an oxygen deficient tissue, oxygen is dissociated from hemoglobin and diffused into the tissue. The 02 is the terminal electron acceptor in the process called oxidative phosphorylation in the production of ATP (Cooley and Lee, 1925).. The removal of 02 turns the iron into its reduced form. The oxygen-unbound hemoglobin is referred to as deoxyhemoglobin. Oxidation of Fe2+ into Fe3+ creates methemoglobin which cannot bind with O2.

Hemoglobin is a carbon dioxide carrier

Hemoglobin also transports carbon dioxide from tissues to lungs. 80% of the carbon dioxide is transported via plasma (Lichtman et al., 2000) Carbon dioxide does not compete with the oxygen-binding site of hemoglobin. It binds to the protein structure other than iron-binding positionThe carbon dioxide bound hemoglobin is referred to as carbaminohemoglobin.

Hemoglobin gives the red color to blood

Hemoglobin gives a red color to red blood cells by Fe2+ ions. With red blood cells, blood reaches to its unique red color. Plasma, without red blood cells, has a pale yellow color. (Naderi and Tabibian, 2014).

Hemoglobin maintains the shape of the red blood cells

The shape of the red blood cells is maintained by hemoglobin. Red blood cells are biconcave disks which are flattened and depressed in the center. They have a dumbbell-shaped cross section. Hemoglobin gene also consists of various alleles. Most mutants may cause no disease. But some mutants may cause hereditary diseases like hemoglobinpathesis (Muncie and Campbell, 2009).

Hemoglobin acts as a buffer

Hemoglobin maintains the blood pH at 7.4. Accumulation of carbon dioxide in the blood decreases the pH from 7.4. The change of the pH can be reversed by ventilation. Due to this buffering action of hemoglobin, all the enzymatic reactions in the body, which prefers this pH, can take place without any disturbance (Borgna and Galanello, 2009).

Types hemoglobin

The most common types of normal hemoglobin are:

Hemoglobin A. This is the most common type of hemoglobin found normally in adults. Some diseases, such as severe forms of thalassemia, may cause hemoglobin A levels to be low and hemoglobin F levels to be high (Weatherall, 2010).

Hemoglobin F (fetal hemoglobin). This type is normally found in fetuses and newborn babies. Hemoglobin F is replaced by hemoglobin A (adult hemoglobin) shortly after birth; only very small amounts of hemoglobin F are made after birth. Some diseases, such as sickle cell disease, aplastic anemia, and leukemia, have abnormal types of hemoglobin and higher amounts of hemoglobin F.

Hemoglobin A2. This is a normal type of hemoglobin found in small amounts in adults (Danjou et al., 2012). There are more than 350 types of abnormal hemoglobin The most common are : Hemoglobin S. This type of hemoglobin is present in sickle cell disease. Hemoglobin C. This type of hemoglobin does not carry oxygen well. (Noetzli et al., 2012) Hemoglobin E. This type of hemoglobin is found in people of Southeast Asian descent. 4-Hemoglobin D. This type of hemoglobin is present in some sickle cell disorders. (Gedara et al., 2012).

Thalassemia

Thalassemia Thalassemia is a group of hereditary blood disorders due to absent or reduced production of hemoglobin which protein present in erythrocytes responsible for carrying oxygen throughout the body. Each erythrocyte may contain between 240 and 300 million molecules of hemoglobin. A hemoglobin molecule has two sub-units usually indicated to as alpha and beta. Both sub-units are necessary to bind oxygen and deliver it to cells and tissues in the body. The gene that controlled the production of alpha chains is called the alpha globin gene cluster, and similarly the beta globin gene produced beta chains. A lack of a particular subunit detects the type of the resulting thalassemia (alpha or beta) (Birgens, 2007).

Types of thalassemia

The two common kinds of thalassemia are alpha and beta. There are many several kinds of alpha thalassemia, such as silent carrier alpha thalassemia has been the most prevalent kind. There are two genes on every chromosome (16). One of it's alpha gene is absent with in silent carrier condition, leaving three of the four genes (aa/ao)(Piel & Weatherall, 2014

Alpha thalassemia trait, this form is usually caused by the deletion of two alpha genes on one chromosome 16 (aa/oo) or the deletion of one gene from each chromosome 16 (ao/ao). Thalassemia trait is more common in southeast Asia, some parts of a middle east, and the Indian subcontinent. This trait is characterized by mild anemia (Huang et al., 2020).

Hemoglobin H disease, this form results of deletion or inactivation of three alpha globin genes (oo/ao), resulting also in an abundance of beta chains. Patients usually present with severe anemia, splenomegaly, icterus, and abnormal red blood cell indices (Farashi & Harteveld, 2018). Alpha thalassemia major, this condition results from the deletion of all alpha genes on both copies of chromosome 16 (o0/00), leading to the severe form of homozygous alpha thalassemia. This condition is usually incompatible with extra uterine life and results in hydrops fetalis and death shortly after delivery unless intrauterine blood transfusion is given (D. Z. Li & Yang, 2017)

Beta Thalassemia in contrast to the duplication found in alpha thalassemia, there is only one beta-globin gene on chromosome(11) (Cappellini, 2012). Beta-thalassemia minor or beta silent carrier is the most common form of beta-thalassemia. There are frequently no symptoms but have small alterations in the number or size of red blood cells in these patients (Jha R & Jha S, 2014). Beta thalassemia trait or beta thalassemia intermediate. In this condition, the production of beta- globin is decreased. Patients have mild anemia, abnormal red blood cell indices, and abnormal hemoglobin electrophoresis results with elevated levels of Hb A2, Hb F, or both (Lohani et al., 2018). Thalassemia major (Cooley's anemia), in this condition, the patient cannot produce beta- globin. To compensate, the marrow produces gamma globin and more alpha-globin. This illness is marked by transfusion- dependent anemia, large splenomegaly, growth retardation, bone abnormalities, and unique facies. Electrophoresis of hemoglobin reveals a high quantity of Hb F, Hb A2, and no Hb A (Al-Allawi et al., 2014).

Complications of Thalassemia

Skeletal Changes

Red blood cell (RBC) production occurs primarily in the bone marrow. In the case of thalassemia, this RBC production is ineffective. One way the body attempts to improve production is by expanding the available space in the bone marrow. This most notably occurs in the bones of the skull and face. Early initiation of chronic transfusion therapy can prevent this from occurring.

Splenomegal

The spleen is capable of producing red blood cells (RBC); it generally loses this function around the fifth month of pregnancy. In thalassemia, the ineffective RBC production in the bone marrow can trigger the spleen to resume production. In an attempt to do this, the spleen grows in size (splenomegaly).

Gallstones

Thalassemia is a hemolytic anemia, meaning the red blood cells are destroyed more rapidly than

they can be produced. Destruction of the red blood cells releases bilirubin, a pigment, from the red blood cells. This excessive bilirubin may result in the development of multiple gallstones.

Iron Overload

People with thalassemia are at risk for developing iron overload, also called hemochromatosis. Excessive iron comes from two sources: repeated red blood cell transfusions and/or increased absorption of iron from foods. Iron overload can cause significant medical problems in the heart, liver, and pancreas.

Heart and Lung Issues

Heart issues are not uncommon in people with beta thalassemia major. Enlargement of the heart occurs early in life due to anemia. With less blood, the heart needs to pump harder, causing enlargement. Transfusion therapy can help prevent this from occurring.

Endocrine Problems

The excessive iron overload in thalassemia can result in iron being deposited in the endocrine organs, such as the pancreas, thyroid, and sex organs. Iron in the pancreas can result in the development of diabetes mellitus Iron in the thyroid can cause hypothyroidism (Husna., 2017).

Diagnosis of thalassemia

Like any other disease, it requires several important stages in its diagnosis which are family and clinical history and laboratory tests.

Clinical and family history:

Diagnosis of hemoglobinopathy is not only based on laboratory tests but also includes Clinical and family history of patients Testing family members is an important part of the diagnostic process. Clinical examinations depend on the type of thalassemiaSimple type (thalassemia minor), the patient may not show any symptoms Or show slight signs of paleness due to mild anemia during the first year of life. As for thalassemia intermediate, the second chapter reviews Patient signs showing signs of anemia at late times may arriveFor the second decade of life. As for thalassemia major, it results in severe infection. Anemia that depends mainly on regular blood transfusions. Otherwise, Death is the fate of the patient in addition to other symptoms such as a change in The shape of the bones, especially the bones of the face and cheeks, where Facial features become characteristic of this disease as well as poorAppetite and growth retardation. frequent infections General weakness, enlargement of the liver and spleen. (Soltani et al., 2020).

Blood tests:

One is the CBC (complete blood count) test, which includes measurements of hemoglobin and the amount (and volume) of red blood cells. People with thalassemia have blood cells. The most important indication of thalassemia is a decrease in the average red blood cell volume (MCV), and it is confirmed by other laboratory tests. less healthy red and hemoglobin less than normal; People with alpha or beta thalassemia trait may have smaller than normal red blood cells.

Hemoglobin check

The examination for thalassemia is also done through a hemoglobin test. The type and percentage of hemoglobin in red blood cells is determined. In the normal situation, the hemoglobin percentage in adults is as follows: Hemoglobin A in the alpha and beta chains constitutes 95-98%. Hemoglobin A2 makes up 2-3%. Hemoglobin F is less than 2%. Genetic test:

If you are pregnant or have a baby, you can have tests done to see if your baby will develop this condition. Genetic testing can show whether you or your partner carry any of the genes that cause thalassemia. A chorionic villus sampling tests a small piece of the placenta to see if the baby has the genes that cause thalassemia. (Al-tamemi, 2019) Doctors usually do this test around the 11th week of pregnancy. Amniocentesis tests the fluid around the fetus. Doctors usually perform this test around the 16th week of pregnancy. (Husna et al., 2017). Newborn examination:

Moderate to severe thalassemia is often diagnosed in childhood because symptoms usually appear within the first two years of a child's life. If your

doctor suspects your child has thalassemia, they can confirm the diagnosis with blood tests.

DNA Analysis:

This test is done to confirm the occurrence of genetic mutations, and to determine the type of mutation, and its location on the hemoglobin chains.This test is not done routinely, but it is used in the final diagnosis of thalassemia (Arvia et al., 2020).

Treatment

1-Blood Transfusion:

It is the mainstay of care for individuals with thalassemia. The purpose of transfusion is twofold: to improve anemia and suppress ineffective erythropoiesis. Chronic blood transfusions prevent most serious developmental, skeletal, and neurological complications of thalassemia. However, once initiated, transfusion-related complications become a major source of morbidity. Standards should be developed to ensure a safe approach to the use of blood transfusions in the management of these disorders(Jha S, 2014).

bone marrow transplant:

It is one of the treatment methods used in the treatment of thalassemia cases main After early diagnosis of the disease also, this method can provideThe cure rate is more than 80% of case s (Winichakoon, 2015).

treatment attempts:

Thalassemia started as such in 1981 AD with more than 1500 cases. This method involves taking bone marrow from healthy individuals(donors) who donate their marrow to patients (recipients), andPatients' marrow is first destroyed by drugs or radiation through an operation called bone conditioning.

Splenectomy

Splenectomy is indicated in a transfusion-dependent patient when hypersplenism increases transfusion requirements and prevents adequate body iron control. An enlarged spleen - without a concomitant increase in transfusion requirements - is not necessarily an indication for surgery.

Supportive treatment

A- Desferrioxamine:where iron increases in blood cells in patients with thalassemia, which leads to an increase in ironpregnancy "and becomes a toxic element for tissues and organs, especiallyLiver and heart, because excess iron leads to early death. Patient due to organ failure, and to help remove excess iron is givenTo the patient (iron chelation therapy), a drug given to the bodyIt combines with excess iron and removes it through urine or feces.

B- Folic acid: Folic acid is given to thalassemia patients along with blood transfusions and iron chelation drugs to help build red blood cells and strengthen the blood. (Aggarwal, 2014). gene therapy Adding a functional gene to the defective blood stem cells is a successful treatment for patients with severe thalassemia. (Talwar, 2016).

Recomme Dation For Patient with Thalasemia:

- Staying healthy: Erythromycin if you or, A daily antibiotic is usually recommended (penicillin important to protect against serious are allergic to penicillin) This is especially infections in children aged under 5 years.
- Immunisations: all the usual childhood vaccinations are advised, you should have vaccinations against meningitis and hepatitis a flu(influenza). These vaccines are recommended both for adults and for children with thalassemia.
- Vitamin supplements: extra folic acid is usually recommended. This helps the body to make new red blood cells. Avoid smoking (which is bad for blood vessels) and excess alcohol. Avoid factors which can trigger sickling.

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