وزارة التعليم العالي والبحث العلمي

جامعة الفرات الأوسط التقنية

المعهد التقني الطبي الكوفة

القسم: صحة المجتمع

(دراسة توزيع فصائل الدم ABO لدى بعض مرضى الثلاسيميا في محافظة النجف الأشرف)

بحث التخرج مقدّم إلى المعهد التقني الطبّي قسم تقنيات صحة المجتمع جامعة الفرات الأوسط التقنية من أجل إستيفاء متطلبات درجة الدبلوم

من قبل الطلبة :

محمد صادق فاضل عبد العباس
مقتدى رياض حمزة
محمد حسن علي
مرتضى انور صباح
كرار حيدر مجيد
عباس رعد شمران

عباس عماد عواد
غزوان عباس كريدي
غسق احمد رياض
غدير واثق نعمة
فاطمة فارس عبد الكاظم
فاطمة فلاح كاظم

زينب احمد حبيب
زينب غانم راضي
زينب مزهر رحيم
هيام لطيف عبد الامير
ولاء سامي حميد

إشراف:
م.د نور إبراهيم عبد الزهرة

1446ه 2025م

بِسْمِ اللَّـهِ الرَّحْمَـٰنِ الرَّحِيمِ

{ يَرْفَعِ اللَّهُ الَّذِينَ آمَنُوا مِنكُمْ وَالَّذِينَ أُوتُوا الْعِلْمَ دَرَجَاتٍ } سورة المجادلة : الآية 11

صدق الله العلي العظيم

الإهداء:

أولاً: نتقرب إلى الله عزَّ وجلَّ بهذا العمل المتواضع

ونهدي هذا العمل والجهد لرسولنا الكريم صلى الله عليه وآله وسلم

وإلى أمير المؤمنين الإمام علي عليه السلام

وإلى مولانا صاحب العصر والزمان عجل الله فرجه الشريف

وإلى الآباء والأمهات الفاضلون

والى كل طلبة العلم

وأيضاً الساهرون من أجل أمان وراحة أبناء هذا الوطن

ونخص بالذكر شهدائنا الكرام.

إقرار المشرف:

أشهد أن إعداد مشروع البحث الموسوم (دراسة توزيع فصائل الدم ABO لدى بعض مرضى الثلاسيميا في محافظة النجف الأشرف)

للطلبة المدرجة أسمائهم أدناه قد تم تحت إشرافي في قسم تقنيات صحة مجتمع ..

محمد صادق فاضل عبد العباس	عباس عماد عواد	زينب احمد حبيب
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كرار حيدر مجيد	فاطمة فارس عبد الكاظم	ولاء سامي حميد
عباس رعد شمران	فاطمة فلاح كاظم	

المشرف : م.د نور إبراهيم عبد الزهرة

التوقيع:

التاريخ:

توصية رئيس القسم

بناءً على توصية م. د. نور ابراهيم عبد الزهرة شبر أُحيل مشروع التخرج هذا إلى لجنة المناقشة.

رئيس القسم : م. أحمد عبد الحسن محسن

التوقيع :

التاريخ :

The Republic of Iraq

Ministry of Higher Education

and Scientific Research

Al-Furat Al-Awsat Technical University

Technical Institute / Kufa

Community Health Department

A study to find the distribution of ABO blood group in some beta thalassemia patients in Al-Najaf Governorate.

Graduation research submitted to the Technical Medical Institute, Department of Community Health Technologies, Al-Furat Al-Awsat Technical University, in order to fulfill the requirements for a diploma degree

Supervised by
Dr: Noor Ibrahim Abdul Zahra

Abstract:

Beta thalassemia (ß-thalassemia) is an inherited hematological disorder involving decreased amount of hemoglobin production. It is a major problem of concern causing high mortality rates in children. Thalassemia patients suffer from severe anemia due to which they need to get repeated blood transfusion after a regular period of time. Many studies have reported association of ABO blood group with diseases. **AIM AND OBJECTIVES:** - To study the relation between the ABO blood group and beta thalassemia. **MATERIALS AND METHODS: -** This was a cross sectional, observational survey-based on study conducted at of AL-Zahraa Teaching Hospital Thalassemia Care Centre,Al-Najaf City. The study was conducted on 50 registered beta thalassemia major patients during February 2025 to Abril 2025. These patients visited the thalassemia care center for repeated blood transfusion. Blood group of the patient was determined by Slide Agglutination Method. **Results** were prepared & tabulated in Microsoft Excel 2010. Where It is found that among the study that females were more affected than males. It is more prevalent in Rh positive individuals as compared to Rh negative. Frequency of blood groups affecting patients were A>O>B>AB. **CONCLUSION:** - Thalassemia is more prevalent in females than males. The most commonly affected blood group is A positive followed by O positive, B positive and last AB positive. Among the Rh blood group, Rh positive were more as compared to Rh negative .

الخلاصة :

الثلاسيميا بيتاβ(الثلاسيميا) او فقر دم البحر الابيض المتوسط هي اضطراب دموي وراثي يتسم بقلة إنتاج الهيموجلوبين. تمثل مشكلة رئيسية تؤدي إلى معدلات وفيات مرتفعة لدى الأطفال. يعاني مرضى الثلاسيميا من فقر الدم الشديد، مما يستدعي ضرورة تلقيهم عمليات نقل دم متكررة على فترات منتظمة. وقد أفادت العديد من الدراسات بوجود علاقة بين مجموعة الدم ABO والأمراض.

الهدف والأغراض: دراسة العلاقة بين مجموعة الدم ومرض البيتا ثلاسيميا

المواد والطرق: كانت هذه دراسة مسحية قائمة على الملاحظة ومنهج مقطعي أجريت في مركز رعاية الثلاسيميا بمستشفى الزهراء التعليمي في مدينة النجف. تم تنفيذ الدراسة على 50 مريضًا مسجلًا يعانون من الثلاسيميا بيتا الكبرى خلال الفترة من فبراير 2025 إلى أبريل 2025. كان هؤلاء المرضى يزورون مركز رعاية الثلاسيميا لتلقي عمليات نقل الدم المتكررة. تم تحديد مجموعة الدم للمرضى باستخدام طريقة حساب النسب المئوية. تم إعداد النتائج وتجميعها في برنامج مايكروسوفت إكسل 2010. وقد أظهرت النتائج أن الإناث كانوا أكثر تأثرًا من الذكور، وأن المرض أكثر شيوعًا بين الأفراد ذوي فصيلة الدم A وكذلك بالنسبة للعامل الريسي Rh فكانت نسبة الايجابي اكثر من السلبي.

الاستنتاج:

تنتشر الثلاسيميا بشكل أكبر في الإناث مقارنة بالذكور. وأكثر فصيلة دم تأثرت هي Aإيجابي، تليها O إيجابي، ثم B إيجابي وأخيرًا AB إيجابي. أما بين فصائل الدم Rh، فكانت فصائل Rh إيجابي أكثر شيوعًا مقارنة بـ Rh سلبي.

Introduction

Thalassemia is a group of inherited blood disorders and one of the most common hemoglobinopathies worldwide [1]. It is classified into two main types: Alpha and Beta Thalassemia [2]. These conditions are caused by genetic mutations that lead to a deficiency or dysfunction of α and β globin proteins, respectively. In some instances, one of these proteins may be entirely absent [3]. The α and β globin chains form a pocket for heme (Fe++) binding, essential for oxygen transport [2]. The genes encoding these globin proteins are located in clusters on chromosomes 16 and 11, respectively. Different globin genes are expressed at various stages of life, with γ globin proteins partnering with α globin during embryonic and fetal development, later being replaced by β globin proteins [4]. An imbalance in globin chains causes hemolysis and disrupts erythropoiesis, Mild symptoms are typically seen in carriers or individuals with the alpha or beta thalassemia trait [5]. Alpha thalassemia can lead to conditions such as hemolytic anemia or severe hydrops fetalis, depending on disease severity. Beta thalassemia major causes hemolytic anemia, growth retardation, and skeletal abnormalities in early childhood, and affected children require regular blood transfusions [6] . However, frequent transfusions can result in iron overload, leading to complications such as renal or hepatic dysfunction. As a result, thalassemias are now recognized as a syndrome. The only potential cures currently available are bone marrow transplants or gene therapy, but these have not yet achieved significant success rates. A deeper understanding of the molecular mechanisms underlying thalassemia may open up new avenues for treatment, as a permanent cure remains elusive even after over 87 years of research since its initial description in 1925 [1].

In 1925, Dr. Cooley, a dentist, first reported a progression of iron deficiency in infants, leading to symptoms such as splenomegaly and bone deformities shortly after birth [1] [2]. Seven years later, in 1932, Whipple and Bradford provided the first explanation of the disease's pathology. Since many affected patients were from the Mediterranean region, they named the condition "thalassemia" [7].

Key world : thalassemia, fetal , Rh ,iron

Chapter tow Literature review

Literature review

Thalassemia is a complex group of hereditary disorders in which the insufficient production of at least one globin chain causes an imbalance in globin-chain production, resulting in damaged hemoglobin and ultimately anemia [4].

Thalassemia also refers to blood disorders caused by the reduced levels or absence of normal globin chains in the hemoglobin protein of red blood cells. There are four main types of globin chains: alpha (α), beta (β), gamma (γ), and delta (δ). Depending on which chain's production is disrupted, thalassemias are classified as α-, β-, γ-, δ-, δβ-, or εγδβ-thalassemias, Most thalassemias are inherited as recessive traits, with the most common forms being α- and β-thalassemias. These result from deficiencies in α- or β-globin proteins, which are essential for producing the normal hemoglobin molecule (HbA, α2β2) in adults [3]. Hemoglobin, a metalloprotein found in the red blood cells (RBCs) of all vertebrates (except for the Channidae fish family) and certain invertebrates, functions as an oxygen carrier [7]. It transports oxygen from the lungs or gills to body tissues, where it unloads the oxygen for use in aerobic respiration to generate ATP, which powers metabolic processes [5]. Each hemoglobin molecule in mammalian RBCs can bind up to four oxygen molecules, increasing the blood's oxygen-binding capacity by seventy times, with a hemoglobin oxygen-binding capacity (OBC) of 1.34 O2 mL/gm Hb [6]. A small portion of oxygen also dissolves directly into the blood during respiration, but this represents only 1.5% of the total oxygen carried [7]. In addition to oxygen, hemoglobin also helps transport other gases, such as carbon dioxide (CO2), which is produced during metabolic activities. Hemoglobin binds some of the CO2 in the form of carbaminohemoglobin, contributing 20–25% of the CO2 exhaled [8]. Additionally, hemoglobin carries nitric oxide (NO), an important regulatory molecule, by binding it to a thiol group on the globin protein and releasing it alongside oxygen [9].

Hemoglobin is not only found in red blood cells, but can also be found in red blood cell progenitor cells, A9 dopaminergic neurons in the

ventrolateral midbrain of some rodents and primates, macrophages, alveolar cells, and mesangial cells that support the glomerular tuft within the kidney, other cells that contain hemoglobin. In these tissues, hemoglobin acts as an antioxidant and somewhat of a metabolic regulator rather than providing oxygen [8].

The functional and practical exercises performed by hemoglobin other than gas transport include fertilization, signaling, and modulation of inflammatory reactions to defend and protect the cell. These exercises are performed efficiently while hemoglobin is safely contained within the boundaries of the red blood cell. Outside the boundaries of the red blood cell, hemoglobin breaks down and puts the life of the cell at risk as in severe cases, antioxidants become overloaded to remove the free radicals that are produced during the oxidation of hemoglobin [10].

Hemoglobin is a protein consisting of four polypeptide subunits with a molecular weight of 64,500 Daltons. It consists of two alpha chains and two beta chains, each containing 141 and 146 amino acids, respectively (Figure 1). In adults, the secondary structure of hemoglobin for all polypeptide chains is essentially an alpha helix. Hemoglobin A does not contain any beta strands or disulfide bonds. It also unusually lacks isoleucine. The beta chain of hemoglobin A consists of eight helical fragments, designated by the letters A through H. The alpha chain is quite similar but lacks the D helix. Each polypeptide chain of hemoglobin A maintains a three-dimensional configuration, known as a globin fold, just like the closely related monomeric protein, myoglobin (Mb). The globin fold is actually an arrangement of helices that form a cavity that holds and attaches a prosthetic heme (Fe++) group. There is a covalent bond between the NƐ2 atom of the F8His residue and the heme iron within each polypeptide of the globin subunits. This heme/iron atom in the ferrous state has the ability to bind reversibly to a specific gaseous ligands like oxygen, carbon monoxide, and nitric oxide [11]. As already mentioned, hemoglobin comprises two α and two β-chains. Therefore, it can be said that it is a dimer of alpha-beta dimers (αβ dimers). The α1β1 and α2β2 dimers are connected by a 2-crease pivot of symmetry. The interfaces of subunits α1β1 and α2β2 are identical, and α1β2 and α2β1 subunit interfaces are mirror images of each other [12].

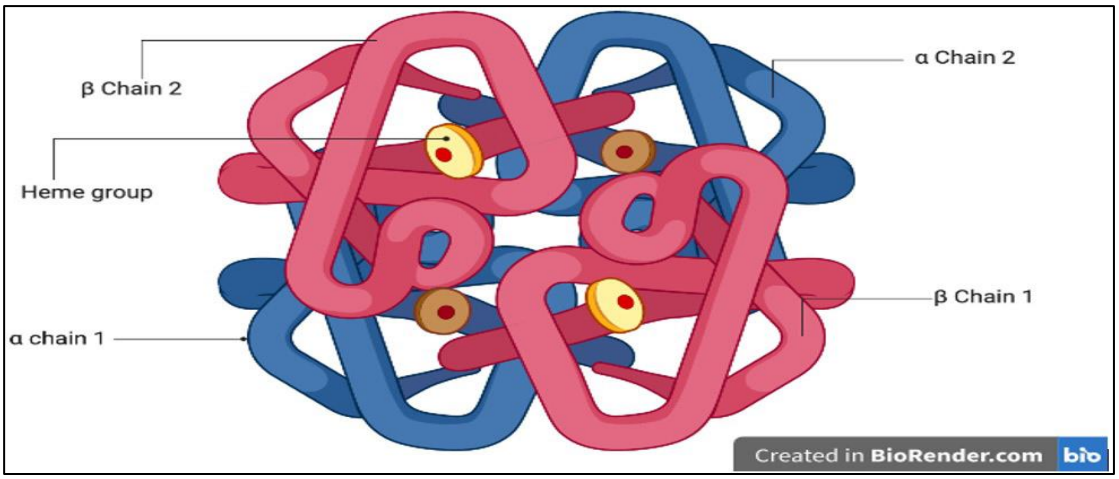

Figure 1. Ultrastructure of the hemoglobin molecule.

The human embryo and fetus normally develop with different hemoglobin variants i.e., Hb Portland-1 (ζ2γ2), Hb Gower-1 (ζ2ε2), Hb Gower-2 (α2ε2) and fetal Hb or HbF (α2γ2) [13]. Stage-specific combinations of globin genes are transcribed within the fetus during gestation, which leads to producing various forms of hemoglobin molecules such as several embryonic hemoglobins, hemoglobin A (HbA) and, hemoglobin F (HbF) Immature erythrocytes produce the embryonic hemoglobins (Gower 1, Gower 2, and Portland) in the yolk sac. They persist up to the 12th week of pregnancy. In the fifth week, Hemoglobin F (Hb F) appears which predominates during fetal life. Hb F is synthesized initially in the liver of the fetus and remains there for several weeks after birth. HbA prevails after birth, which originates in the bone marrow. Most common among other variants is Hemoglobin A (α2β2) usually with an amount of around 95% [14]. The normal range of hemoglobin A2 (α2δ2) is 1.5–3.5% of the total hemoglobin in an adult. Though Hb A2 has no physiological importance in an adult its level may rise in case of alpha or beta chain reduction [15] the mutations in delta globin genes along with beta-globin gene variations may also interfere with the beta-thalassemia diagnosis especially in the cases of beta-thalassemia trait [15]. The gamma chain is synthesized late in the last trimester and at this stage, the Hb F (α2γ2) is only restricted in a small number of RBCs known as ‘F-cells’. Interestingly, in individuals having

sickle cell anemias and beta-thalassemia, the Hb F level is quite elevated [14].

1 .Alpha thalassemia

There are two copies of the alpha globin gene in the human genome, both located on chromosome 16, so in a normal diploid cell, 4 copies of the gene are available to produce the protein. Alpha thalassemia is caused by the lack of alpha globin protein production due to a mutation or deletion of one of the four alpha globin genes [16].

Two phenotypes of α-thalassemia have been identified so far: α-thalassemia I (or minor) and α-thalassemia II, the latter of which shows no clinical symptoms of the disease. It is now understood that α-thalassemia I is associated with the complete absence of α-globin proteins, while α-thalassemia II is characterized by a reduction in the expression of α-globin. These two variants are now referred to as thalassemia α° and thalassemia α+, respectively. [17].

Alpha (0) thalassemia – there are more than 20 different mutations described, resulting in the deletion of all the sets of α-globin genes. People having this deficiency are unable to synthesize normal α-globin and therefore cannot make any normal functioning A, F, or A2 hemoglobin. This prompts the onset of hydrops fetalis or “hemoglobin Bart”; children born with this disorder do not survive outside the uterus.

Alpha (+) thalassemia –more or less fifteen genetic mutations are reported, which result in limited α-globin protein synthesis generally because of the functional deletion of at least one alpha-globin gene. Alpha (+) thalassemia is further sub-classified into four categories:

A- Thalassemia (-α/αα) occurs when three out of four functional α-genes are inherited. The individuals are referred to as asymptomatic carriers for α-thalassemia. Various terms used for this disorder are “alpha thalassemia minima”, “alpha thalassemia-2 trait”, and “heterozygosity for alpha (+) thalassemia minor”. These carriers are clinically normal or may have mild anemia;

B- Thalassemia (-α/-α) condition is known as a transdeletion because two healthy alpha genes are inherited, one from each of the two chromosomes

(-α/-α) whereas homozygosity for alpha (+) thalassemia (αα/--) (two on the same chromosome) is known as a "cis deletion" resulting in "alpha thalassemia minor" or "alpha thalassemia-1 trait". Parents who are carriers of the cis deletion can have one out of four (25%) babies affected with alpha thalassemia major in every pregnancy;

C- Hemoglobin H: when only one healthy alpha gene (-α/--) is inherited, it results in the massive production of hemoglobin H (Hb H) comprising tetramers of surplus beta chains. The disorder is named "Hb H disease";
D- Hemoglobin Bart's disease: When all four alpha genes are lost, a situation occurs, that is life-threatening. Four gamma-globin chains are formed during the life of the fetus inside the womb which unites to frame irregular hemoglobin known as 'hemoglobin Bart's' [18].

Alpha thalassemia differs from beta thalassemia in its pathophysiology. The deficiency of the alpha chain results in the overproduction of gamma or beta chains, which form hemoglobin Bart and hemoglobin H, respectively. These soluble tetramers do not accumulate in the bone marrow, and thus the process of erythropoiesis is more viable compared to beta thalassemia. However, hemoglobin H is not only unstable, but also accumulates in red blood cells over time. The inclusion bodies thus generated are captured in the spleen and various parts of the microcirculation, leading to reduced red blood cell survival. Moreover, both hemoglobin Bart and hemoglobin H have very high oxygen affinity; due to the absence of alpha chains, there is no heme-heme interaction and their oxygen dissociation curves resemble myoglobin [19]. In conclusion, there are four subtypes of alpha thalassemia ranging from moderate to severe in their effects on the patient's body [20].

1. Alpha thalassemia minor It is an asymptomatic carrier condition that occurs due to the deletion of the one α- globin gene. This condition usually causes no symptoms or signs of anemia and does not need treatment due to negligible alpha protein deficiency; therefore, the hemoglobin appears to be normal [16]. The term "silent carrier" is usually used to describe this condition because it is not easily diagnosed through standard hematological investigations. Only DNA analysis could detect this condition [21].

1.2. Alpha thalassemia trait The trait is also known as mild alpha-thalassemia. The patients are deficient in two alpha-globin genes. The affected individuals have RBCs smaller than usual and are mildly anemic

but do not show any symptoms and may only be diagnosed by routine tests [16].

1.3. Alpha thalassemia intermedia Also, it is known as hemoglobin H disease. Individuals lacking three alpha globin genes become severely anemic and mostly cannot survive without blood transfusion. Newborns who inherited alpha thalassemia intermedia seem healthy at birth but mainly develop anemia and splenomegaly as they approach the second year of his life. Hepatomegaly is not commonly reported, and there might be some relationship to the mental retardation in affected individuals. As hemolysis occurs in this type of anemia the tendency to develop respiratory infections, gallstones, and leg ulcers increases. Bone deformities are not usually found in hemoglobin H disease [20]. The imbalanced alpha and beta chain synthesis (that is usual) induces aggregation of beta chains inside the RBCs. Usually, beta chains are coupled with alpha chains only. Alpha thalassemia with three-gene deletions causes the beta chains to accumulate in gatherings of four, creating unusual hemoglobin, called "hemoglobin H". This condition leads to "hemoglobin H disease". This hemoglobin variant has two issues. First, it does not convey oxygen efficiently, making it practically useless to the cell. Secondly, hemoglobin H protein harms the cell membranes of RBCs, accelerating cell death. A combination of reduced alpha chain synthesis and red cell lysis in hemoglobin H disease creates severe and fatal anemia. Without treatment, most individuals do not survive and expire in their early teens or before [21].

1.4. Alpha thalassemia major "Hydrops fetalis" or alpha thalassemia major is a condition in which no alpha genes are found in the patients' genome, resulting in four gamma-globin chains production by the fetus that produces malfunctioning hemoglobin known as hemoglobin Bart's. Most affected individuals having Hemoglobin Bart's cannot survive or otherwise die in just a few hours after birth [20]. Alpha thalassemia with four deletions in the gene has rarely been diagnosed in the uterus, especially in a family with a history of the disorder occurring in early childhood. Reportedly, some of these children have been saved through blood transfusions during pregnancy [21].

2. Beta Thalassemia Around 200 mutations of the beta-globin gene have been identified worldwide which produce beta-thalassemia. Unlike alpha thalassemia syndromes where deletion is usually the root cause, beta-thalassemia occurs due to mutations that influence all stages of beta-

globin protein synthesis including transcription, translation, and beta-globin production durability. Two types of β-thalassemia, ß+, and ß° thalassemia are identified so far that lack beta chain production altogether Beta thalassemia major usually results when ß+ or ß° thalassemia occurs in homozygous condition. Occasionally, however, the compound heterozygous state for both ß+ and ß° thalassemia results in beta-thalassemia. In the case of homozygous ß° thalassemia, there is no Hb A, an abundance of HbF, and variable amounts of Hb A2. In individuals with homozygous ß+ thalassemia, the amount of Hb A is variable, Hb F is increased and distributed heterogeneously among RBCs whereas Hb A2 is normal, decreased, or elevated [22]. The molecular variations in β thalassemia result in missing or diminished β chain generation. Alpha chain Synthesis remains unaffected, and therefore there is an unequal amount of globin chain generation that prompts an abundance of α chains. They are not stable in the absence of their normal partners and precipitate in the RBC precursors, which interferes with RBC processing. As a result, there is a variable level of intramedullary destruction of RBCs precursors (i.e. ineffective erythropoiesis). The RBCs having α chain incorporated when enter the bloodstream interfere with their segment via microcirculation, exclusively in the spleen. Such cells demonstrate a high variability in the structure of membrane and penetrability and are short-lived. Hence, anemia occurs due to both abnormal erythropoiesis and shortened cell survival. The anemia stimulates erythropoietin production resulting in bone marrow expansion, which consequently causes deformed skull and large bones ref needed. Since the spleen is overburdened and required to remove a continuous stream of abnormal red cells, enlarges before it exhausts ultimately [23]. Generally, three categories of beta-thalassemia have been recognized, ranging from mild to severe by affecting the patient's body.

1.2. Beta thalassemia minor Also known as thalassemia trait due to one of malfunctioning beta-globin genes, but this generally causes no significant problem in the proper functioning of hemoglobin protein [24]. When there is an excess of alpha chains, the mechanism that switches off gamma chain expression does not work effectively, thus the levels of Hb F remain somewhat elevated in these patients. The alpha chains consolidate with the accessible beta chains bringing about diminished levels of hemoglobin rest of the surplus alpha chains empower the over-

production of delta chains [25] Affected individuals have a 1:1 chance to pass the thalassemia minor trait to their child [26]

2.2. Beta thalassemia intermedia A condition where the absence of beta polypeptide in the hemoglobin is sufficient to bring about more extreme anemia and serious medical issues, including shortness of breath, bone disfigurements, mild jaundice, and an enlarged spleen. The condition is characterized by having two abnormal genes in affected individuals while still producing some beta-globin. Depending on the level and functional competence of beta-Globin is a broad range in the clinical severity of this disease [24].

2.3. Beta thalassemia major It is also known as "Cooley's anemia" and is the most severe form of beta-thalassemia with absent beta-globin synthesis thus preventing the production of significant amounts of Hb A. The severe irregularity of globin chain synthesis (alpha >> beta) brings about extreme microcytic hypochromic anemia. Within the RBCs surplus unpaired alpha-globin chains precipitate, this harms the plasma membranes of RBCs and brings about intravascular hemolysis. Besides, premature death/apoptosis/lysis/ necrosis of erythroid precursors reduces the number of RBCs even further. The severe anemia results in hypoxia and the resulting EPO causes hyperplasia in the bone marrow and will lead to extramedullary hematopoiesis [1].

During childbirth, the infant with thalassemia major appears to be healthy. This is because there is a predominance of fetal hemoglobin (Hb F) during gestation. which lacks any beta chains. Anemia starts to appear a few months after birth, as the infant switches over from gamma to beta globulin. The infant's growth retards and often has issues (due to poor oxygen absorbance in the body with significant anemia), episodes of fever to which the severe sickliness inclines the small stature, slow bowel movement, and other intestinal issues. If untreated, it will cause the enlargement of organs like the spleen, liver, and heart, and bones to become weak and brittle. The condition results in death before age twenty [24].

Regular blood transfusions and extensive continuous therapeutic care are required throughout life in this type of anemia. After some time, these successive transfusions prompt iron overload in the body. Without treatment, this overabundant iron will be stored in the liver, heart, spleen, and other organs and could prompt a sudden death due to major systemic

failure [1]. Silent carriers of Alpha thalassemia lack signs or side effects of the disorder. Individuals affected by alpha or beta thalassemia disorders might have a slight iron deficiency. It might be an indication. Side effects might be more adverse in the expecting women, or the people with anxiety, or malnourished. Evidence may include fatigue. This might be the main side effect that a person with beta-thalassemia minor shows. Exhaustion is created by the diminished oxygen-conveying limit of the RBCs, bringing about reduced oxygenation for cells and tissues and causing pale skin tone due to insufficient oxygen in the blood [27].

Over the past three decades, regular blood transfusions have dramatically eliminated the complicity of thalassemia and bone marrow transplantation, enhanced the quality of life-permitting normal development throughout childhood and extended life span. But, transfusion results in a complication due to iron overload [28] Regular blood transfusion leads to iron overload-related complications including hormonal complications such as growth retardation, sexual immaturity, diabetes mellitus, and insufficiency of the parathyroid, thyroid, pituitary, adrenal glands, dilated myocardiopathy, liver fibrosis, and cirrhosis [29];[23].

In non-transfused thalassemic patients, the spleen, liver, heart, and bone marrow become significantly enlarged was stated before. Expansion of marrow cavities and thinning of cortices produce a variety of bone abnormalities in patients who are not optimally transfused [27]. The result of bone biopsies from non-transfused thalassemic patients shows osteoporosis with increased bone resorption, decreased mineralization, and fewer bone-forming sites [29]. Over the past few decades, there has been a tremendous advancement in the field of clinical and genetics research. Many countries have nearly wiped out the disease by making better decisions like mass testing for hemoglobinopathies before marriage or childbirth. Thalassemia is now being considered to be treated beyond bone marrow transplantation which has always been the last hope to survive for a thalassemia patient. Today, allogeneic hematopoietic stem cell transplant (HSCT) from human leukocyte antigen (HLA)-matched sibling or other donors is the only treatment for thalassemia patients with > 90% transfusion independent survival rate in the patients transplanted with sibling matched donors. However, the treatment is possible in the individuals at a very young age. The disease-free survival rate depends upon the factors like HLA- matching, age and iron overloading etc [30].

Scientists have developed better tools to treat genetic disorders like stem cell technology and gene therapy to avoid tissue rejection in recipients. The therapy adds a corrective gene whose product combines with α-globin to produce functional hemoglobin, thereby reversing the ineffective red blood cell production seen in β-thalassemia. However, the technique is much costly (~ $1.6 billion) which could not be easy to afford by the patient's family or the healthcare providers [31]. A novel CRISPR technology to edit faulty genes is a new game changer that showed promising results in disease models that made it a new hope to the diseased. The CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) along with the CRISPR- associated system, Cas (known as Crispr-Cas) is a powerful gene editing tool which has revolutionized the field of molecular biology in terms of gene therapies to treat hereditary genetic disorders. CRISPR Cas system enables programmable targeting of single base insertion or deletion (Indels) at a particular site of the genomic DNA. has successfully used the Crispr tool to edit the hematopoietic stem cells in order to downregulate the B globin gene to reduce the faulty beta globin chains and enhance the reactivation of fetal hemoglobin (G globin protein) to overcome the anemia eventually reducing the blood dependency in the thalassemia patients. The patients under trial were transplanted with these edited stem cells. The trial had shown promising results and no discrepancy has been reported so far [32].

Chapter three
Material & Method

1. **PATIENTANDMETHODS Study Design:** The research was a cross-sectional, observational survey-based study. This means that the researchers collected data at a single point in time from a specific group of patients to analyze their blood groups in relation to beta thalassemia .

2. **Setting**: The study was conducted at the AL-Zahraa Teaching Hospital Thalassemia Care Centre,Al-Najaf City This setting was chosen to focus on patients who regularly visit for treatment .

3. **Participants**: A total of 50 registered patients diagnosed with beta thalassemia major were included in the study. These patients were selected based on their need for repeated blood transfusions, which is a common requirement for managing this condition .

4. **Data Collection**: The researchers obtained informed consent from the patients before conducting the study. Blood samples were taken from the patients to determine their ABO and Rh blood groups. This was done using a laboratory technique known as the slide agglutination method **.**

5. **Data Analysis**: The collected data was analyzed using Microsoft Excel 2010. The researchers expressed the results in terms of mean, standard deviation, and percentage to determine if there were significant associations between blood groups and beta thalassemia, considering a p-value of less than 0.05 as significant **.**

6. **Ethical Considerations**: The study did not require ethical approval as it was conducted in a clinical setting with informed consent from the participants

7. Data were collected on male& female thalassemia patients at the AL-Zahra Hospital in Al- Najaf city from February to March 2024

Chapter Four
Result& desiccation

Results:

The study involved 50 registered patients with beta thalassemia major, conducted over two months from February to Aprils 2025 at a care center in AL-Najaf city .

The analysis revealed that more females (27) were affected by beta thalassemia than males (23), indicating a higher prevalence in females .

Among the patients, the distribution of ABO blood groups was as follows:

- Blood group A was the most common, affecting 82% of the patients.
- Blood group B accounted for 2 %.
- Blood group AB was the least common, affecting 0% of the patients .
- Blood group O accounted for 16%.

Table (1) Percentages of Distribution of ABO group in beta thalassemia patients .

Average	Number of patients	% population
A	41	82 %
B	1	2 %
AB	0	0 %
O	8	16 %
Total	50	100 %
RH blood group		
Rh positive	36	72 %
Rh negative	14	28 %
Gender		
Male	23	46 %
Female	27	54 %
Age (In Year)		
Less than 5	1	2 %
5-15	12	24 %
15-25	25	50 %
25-35	8	16 %
More than 35	4	8 %

The study found that beta thalassemia was more prevalent in individuals with Rh positive blood groups (36 patients) compared to Rh negative (14 patients) .

Age distribution showed that the age from 15-25 years were the most affected group, comprising 50% of the study population (50 patients). The next largest group was children aged 5-15 years, making up 24% (12 patients). The age groups (under 5 years and 25-35,above 35 years) had fewer cases, contributing 2% (1 patients) and 16% (8 patients), 4% (8 patients) respectively .

The results indicated that A positive females were the most commonly affected subgroup, with 44% (22 patients), while O positive females accounted for 10% (5 patients) .

Table (2) Distribution of ABO group in beta thalassemia patients according to gender.

Blood group	**Male**	**Percentage**	**Female**	**Percentage**
A	19	38%	22	44%
B	1	2%	0	0
AB	0	0	0	0
O	3	6%	5	10%
Total	23	46%	25	56%
Rh blood group				
Positive	18	36%	18	36%
Negative	5	10%	7	14%
Age in year				
<4	0		1	2%
5-15	5	10%	7	14%
15-25	11	22%	14	28%
25-35	6	12%	2	4%
>35	1	2%	3	6%

- Overall, the findings suggest that thalassemia is more prevalent in female and among those with blood group A, particularly in Rh positive individuals. This information is crucial for public health policies regarding blood availability for thalassemia patients .

  Amongst all the 3 forms of beta thalassemia, beta thalassemia major have severe expression of the disorder hence they require regular blood transfusion. Thalassemia patients need repeated transfusion so it is necessary to determine the frequency of ABO blood groups. As per our study we found that females were more commonly affected than males which is in agreement with other studies like [32], Khan(2015) and Bejaoui (2013) also found in our studies the prevalence of beta thalassemia was more among Rh positive individuals than Rh Negative individuals [33].

  On contrary we have also found more prevalence among Rh positive females than males particularly A positive (1). The ABO blood group affected were inorder of A>O>B>AB in females and males in our studies which is also found in studies like Sarah [34].

  On contrary we have also found more prevalence among Rh positive females than males. Among the age distribution we found that young (15-25) years are more commonly affected than other age group as this disease is an inherited and occurs in infancy

  [31][16].

Conclusions

Prevalence of Thalassemia: The study concluded that beta thalassemia is more prevalent in females than in males. This finding suggests that gender may play a role in the occurrence of this genetic disorder, which is important for understanding its impact on different populations

Blood Group Distribution: The research identified that the most commonly affected blood group among beta thalassemia patients is A positive, followed by O positive, B positive, and finally AB positive. This order of prevalence indicates that certain blood groups may be more susceptible to the disease, which could have implications for blood donation and transfusion strategies

Rh Factor Association: The study found that beta thalassemia is more prevalent in individuals with Rh positive blood groups compared to those with Rh negative blood groups. This suggests that the Rh factor may be associated with the severity or occurrence of thalassemia, which could be relevant for clinical practices in managing patients

Public Health Implications: The conclusions drawn from this study can help inform public health policies regarding blood availability for thalassemia patients. Understanding the distribution of blood groups among these patients can aid in ensuring that blood banks are adequately stocked with the necessary blood types to meet the needs of those affected by thalassemia

Need for Further Research: The authors suggest that the findings warrant further investigation to better understand the relationship between blood groups and beta thalassemia. This could lead to improved management strategies and better outcomes for patients suffering from this condition.

Recommendation

As a department of community health technologies, we recommend:

- Patients should also receive education about the hereditary nature of the disease. If both parents have thalassemia minor, there is a 1/4th chance that they will have a child with thalassemia major. If one parent has beta-thalassemia minor and the other parent has some form of beta-globin gene defect, i.e., sickle cell defect, they should also be counseled about the possibility of disease transfer to their children. Patients with thalassemias should understand that their disease is not due to iron deficiency and that iron supplements will not cure the anemia; in fact, it will lead to more iron buildup if they are already receiving blood transfusion.
- Biochemical markers of bone metabolism that can be done every
- Early diagnosis and treatment of diabetes mellitus

Chapter six
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