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A Review: Genetic Mutations in Hemoglobin: Sickle Cell Anemia

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An irreversible, heritable change to the nucleotide sequence of a gene or chromosome is referred to as a mutation, or in the method through which such a shift takes place. Small-scale and large-scale mutations fall under the two groups of mutations. When one or more nucleotides are changed, removed, or added, small-scale mutations take place in the DNA. Large-scale mutations are those that arise in a specific region of a chromosome. This type of mutation has the potential to be fatal or cause significant damage, Mutations can be classified as small scale or large scale depending on their influence on the gene structure. Anemia and severe pain are symptoms of the hereditary condition sickle cell anemia. People with the illness have a defective gene that contributes to the creation of the protein hemoglobin, which carries oxygen in erythrocytes. People who carry two copies of the sickle cell gene are more likely to develop sickle cell disease. Sickle cell illness does not afflict people who have only one copy of the sickle cell gene, but their descendants may get it from them.

Keywords: Sickle cell anemia, Hemoglobin, B chain, Mutate, and heredity diseases.

Introduction:

One of the most frequent hereditary disorders in the world is sickle cell anemia. Anemia, severe crises, infections, strokes, and cardiac problems are common among patients. Despite the fact that current therapy has improved patients' quality of life and survival rates, cure can only be accomplished when histocompatible donors are available [1]. Despite the 3 billion nucleotides in the haploid human genome, alterations in only one base pair can have a significant physiological impact. For instance, even the tiniest genetic anomaly can cause sickle-cell anemia. The protein that carries oxygen and gives blood its red hue is called hemoglobin. A single nucleotide change is all that is required for a normal hemoglobin gene to transform into a sickle-cell gene. Despite only affecting one amino acid in the protein chain, this one nucleotide mutation has significant consequences [2].

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Mutation in Hemoglobin

Beta hemoglobin, commonly known as beta globin, is an amino acid chain of 147 amino acids. Sickle-cell disease, as previously mentioned, is characterized by an increase in the body's sickle cell population. Adult hemoglobin (Hb) is made up mostly of HbA and HbA2, with a tiny amount of HbF. Hemoglobin S (HbS) is a structural hemoglobinopathy that affects people. the sickle cell trait, which is a heterozygous state (SCT), It's known as HbAS, and it's characterized by the presence of HbS is present in 30-40% of the population, with the rest being normal. HbA.1 In Sub-Saharan Africa, South and Central America, India, and Southeast Asia, this hemoglobinopathy is fairly frequent. Arab countries in the Middle East and the Mediterranean countries. Its prevalence in India ranges from 1 to 40% [3].

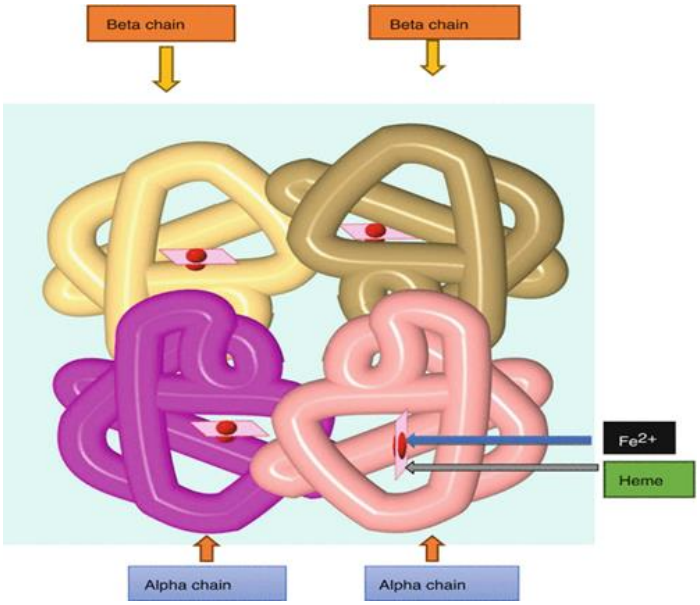

Fig1-1 The typical hemoglobin, which is made up of hem and globin, is depicted as a diagram 2 beta chains and 2 alpha chains) [3].

Genetic inheritance of the sickle cell anemia:

Through forced slavery and current economic migrations, the sickle cell gene has spread across countries and skin hues. SCD has been the focus of intense study and remarkable accomplishments since the discovery of HbS in 1949 [4] have achieved in terms of the pathophysiology's complicated and convoluted pathology. At least three different occurrences in Africa and one in The Senegal, Benin, Bantu, and Indian kinds of sickle cell mutations are assumed to have originated in Asia. A study was conducted in Cameroon to examine if the atypical sickle genes seen in surrounding countries are the product of recombination or the existence of a sickle cell mutation of unknown genetic origin. At the Yaoundé Blood Transfusion Center, it was done on 40 homozygous SS patients who were being monitored [5] [6]. On the 80s chromosomes, 13 chromosomes had a unique polymorphism pattern that appeared three times in the homozygous state. The frame restriction on this chromosome is the AT gene. One amino acid, glutamic acid, is substituted for valine at position six of the 146 amino acids of hemoglobin's beta chain as a result of a genetic mutation that causes sickle cell anemia [7].

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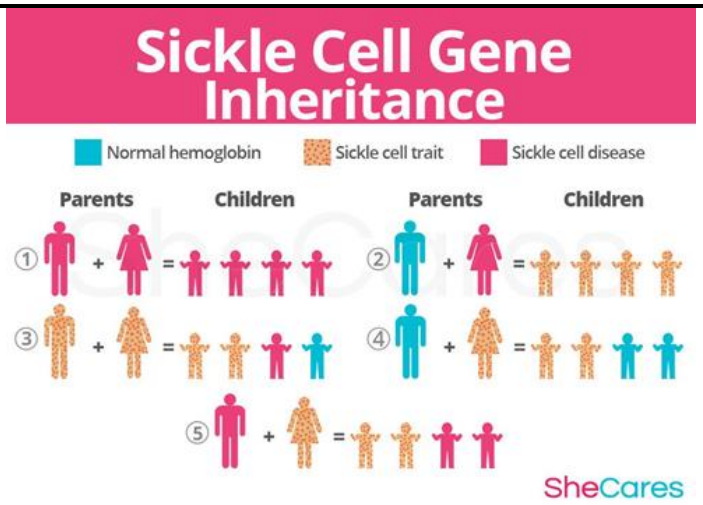

Fig1-2 diagram shown the genetic sickle cell anemia transport [7]

Early diagnose of the disease:

In order to identify the etiology of anemia, diagnostic algorithms often employ the mean cell volume of the erythrocytes (red blood cells), the number of reticulocytes, and the properties of the blood film. This method relies on the presence of a haematology analyzer and a skilled microscopist [8]. Several diseases that cause anemia (e.g., intestinal parasites, malaria, and sickle cell disease) can co-exist in the same person, thus a comprehensive study is necessary to rule out all possible causes of anemia [6]. Screening neonates for sickle cell disease with protein-based methods necessitates confirmation with a liquid blood sample. DNA may be extracted from a sample as small as a perforated disc with a 0.125-inch diameter that contains the equivalent in dried form of around three liters of whole blood. For polymerase chain reaction amplification of the globin region covering the sickle cell mutation, we took DNA from a sample with a diameter of 0.25 inches (12 l equivalent), which allowed us to detect the sickle cell mutation using allele-specific oligonucleotide probes. The expense of obtaining further liquid blood samples would be reduced with molecular confirmation of the original blotter's genotype and the family members would get information more quickly and clearly [9].

Prenatal testing for sickle cell genes:

Amniotic fluid, which surrounds the fetus in the mother's womb, can be sampled in order to identify sickle cell disease in unborn fetuses. The medical personnel must be made aware of or given information about the family's medical history if either parent possesses the sickle cell trait or sickle cell anemia [10] [11].

The risk factors of SCA:

SCA manifests itself clinically in a variety of ways, including anemia severity, the frequency of severe vaso-occlusive episodes, stroke, and death. SCD severity is known to be influenced by both hereditary and non-genetic variables. High fetal hemoglobin (HbF) levels, for example, have long been related with reduced severity [12]. HbF levels are genetically controlled and can be manipulated therapeutically [13]. Similarly, thalassemia co-inheritance protects against certain

SCD-related consequences such hemolysis, stroke, and renal disease. With a decreased estimated glomerular filtration rate, sickle anemia also causes hyperuricemia and nocturnal hypertension (eGFR) [14].

In people with sickle cell anemia, Vaso-occlusion and sudden, intense pain are the outcomes of this complex process. A multicellular collection of platelets, endothelial cells, sickled blood cells and various blood cells, as well as inflammation and adhesion are its defining characteristics. Minimizing the frequency of pain crises and/or avoiding vaso-occlusion, especially in individuals who are more sensitive [15].

Therapies for sickle cell anemia that help to alleviate symptoms:

In most cases, treatment resulted in curative sickle cell therapy, avoiding complications. Surgical therapy is allowed. In certain children and teenagers, stem cells are used to treat this condition [16].

• (Droxia, Hydrea, and Cyclos) Hydroxyurea The incidence of excruciating crises decreases with regular hydroxyurea use, which may also reduce the necessity for blood transfusions and hospital stays. Your likelihood of getting an infection might go up. Do not take any medications if you are expecting.

• L-glutamine oral powder (ENDARY): Currently, the US Food and Drug Administration has approved this drug for the treatment of sickle cell anemia. Furthermore, it assists in reducing the regularity of pain emergencies.

The oral medicine Voxilator (Oxprita) has just received approval from the American Food and Drug Administration to treat anemia in people with sickle cell disease. Adverse reactions include fever, rash, exhaustion, nausea, diarrhea, and headaches [17].

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