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Sickle Cell Disease: A Review

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Abstract

Sickle Cell Disease (SCD) is a hemoglobin disorder that requires lifelong management and contributes to infant, childhood as well as adult morbidity and mortality. SCD is a widespread disease characterized by a variation in the beta-globin gene that results into the production of aberrant hemoglobin called hemoglobin S. The inheritance of the mutation could be homozygous or heterozygous combined with another hemoglobin mutation. SCD can be identified by the presence of dense, sickled cells that grounds for haemolysis of blood cells, chronic anemia, acute painful occurrence, body part alteration, and in many cases death. Early detection/diagnosis of SCD can help to reduce the mortality and management of the disease effectively. Millions of people worldwide are impacted by this prevalent inherited blood disorders, which include sickle cell disease and its variations. Sickle Cell disease results in a markedly reduced life expectancy, particularly in India's tribal people. The review study here explain an overview of the inheritance, severity, pathogenesis, present-day and emergent techniques for SCD detection and highlights the different national & International programs for the elimination of disease from the population.

Keywords: Sickle cell anemia; SCD; Hemoglobinopathies; Detection; Diagnosis; Point of care; National Program; Elimination.

INTRODUCTION

Blood is a special fluid in the body that consists of four main components: plasma, red blood cells, white blood cells and platelets. Hemoglobin (Hb) is a protein molecule found in red blood cells (RBCs) that carry oxygen and provide red blood throughout our body. Normal red blood cells are biconcave, have no nucleus, and are flexible, which helps them move easily through the smallest blood vessels called capillaries. Sickle cell disease is a red blood cell disease caused by a genetic mutation that causes atypical hemoglobin production. This causes red blood cells to lose their normal shape, take on a C shape like a virus or crescent, and fall off easily. These tough, sticky cells can get stuck in small blood vessels and block them, slowing or blocking the flow of blood and oxygen to some parts of the body. It is one of the most common monogenic diseases worldwide with autosomal recessive inheritance (Rees, DC 2010).

Sickle cell syndrome is common and affects 70% of births worldwide. Sickle cell disease (SCD) is a genetic disease caused by mutations in the gene encoding hemoglobin beta subunit (HBB) that can lead to sickle cell anemia (SCA), HbSC, or HbSβ-

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thalassemia (Kato GJ, 2018). Public health in India is a major challenge, especially for tribal people (Colah RB, 2015). SCD is characterized as a somatic chromosomal disorder. Hemoglobin (HbS) allele βS is a hemoglobin subunit β allele in which an adenine-thymine mutation in the sixth codon of β-globin leads to glutamate substitution at position 6 in the β-globin chain with Amino acid replacement to valerin. Although caused by changes in context, its symptoms are also influenced by behavior and environment (Rees DC, 2022). It is a chronic disease that varies in severity and requires lifelong treatment (Brousse V, 2014). (Under 5 years of age) Sickle cell anemia ranks 12th among all causes of death. The highest burden of SCD is reported in Western and Sub-Saharan Africa and India (GBD 2021 Sickle Cell Disease Collaboratives, 2023). SCD is more common across ethnic groups, with a prevalence of 40-55% (Colah RB, 2015). SCD is one of the top ten diseases faced by people in India. However, birth rates in India have fallen from 21% in 2000 to 16% in 2021 (GBD 2021 Sickle Cell Disease Collaboratives, 2023). High risk increases morbidity and mortality in infants and children; Approximately 50-90% of children born with type 2 diabetes die before the age of five (Gyamfi J, 2019). Although influenza is resistant to malaria. This review discusses the etiology and epidemiology of cell disease, its course, major problems, treatment, and future research on the disease.

Sickle Cell Disease: Pathophysiology

Normal red blood cells can survive up to 120 days, but sickle cells can only survive 10 to 20 days. The main pathophysiology is based on the polymerization of deoxygenated HbS and the formation of long fibers in erythrocytes, which causes erythrocyte distortion, resulting in strong hemolysis and vascular occlusion. Additionally, infected cells are destroyed by the spleen due to their shape and hardness. Sickle cells accumulate in these filters and die. When there are fewer healthy red blood cells in the body, a person can become anemic and diseased cells can damage the spleen. Sickle cell anemia causes many problems such as active disease, pain and inflammation in the brain, liver, lungs, etc. It can cause damage to many parts of the body, including (Bunn HF. 1997).

Types of Sickle Cell Disease

Most human hemoglobin A (HbA), also known as adult hemoglobin (hemoglobin A1 or α2β2), consists of two beta globin subunits and two alpha globin subunits. These two genes must function properly and work together to produce normal hemoglobin for human children and adults. When hemoglobin is not properly replaced with normal hemoglobin (HbA), a person may become sick or ill. If normal heme (HbA) is replaced by abnormal hemoglobin, the person may become sick or ill. Sickle hemoglobin (HbS) is the result of mutations in the β-globin chain. If only one beta globin subunit is affected, the person has a good thing, and if both are affected, the person has sickle cell disease. Patients with cancer inherit HbS from one parent and HbA from the other parent, making them heterozygous and causing the disease. People with cancer inherit two HbS genes from their parents, making them homozygous. Sometimes a person can get the beta thalassemia gene from one parent and the cancer gene from the other parent.). This is often called sickle cell anemia/disease and is usually the most severe form of the disease. One parent and one gene for beta thalassemia (another type of hemoglobinopathy). People with HbS beta thalassemia often have severe SCD.

EPIDEMIOLOGY

Sickle cell trait (SCT) is more common in people of African descent and in people whose ancestors came from tropical and subtropical regions where malaria is common. In the United States, 0.2% of whites and 9% of African Americans have breast cancer (Gibson JS, 2016). Approximately 300 million people worldwide have this disease, with sub-Saharan Africa accounting for one-third of this number (El Ariss AB, 2016). Sickle cell trait is more common in areas where malaria is common. According to a study, the prevalence of SCT can reach 25% in some African countries and 60% in Saudi Arabia. SCT and disease prevalence are likely to increase in the western part of the world due to large migration of people from high disease burden regions such as Africa and the Middle East (Rogers ZR, 2023). Many people have been examined in India and according to various studies, the states where SCD is found are: Gujarat, Rajasthan, Uttarakhand, Maharashtra, Bihar, Jharkhand, Madhya Pradesh, Chhattisgarh, Odisha, West Bengal, Tamil Nadu, Telangana, Andhra Pradesh, Karnataka, Kerala. States, Uttar Pradesh and Assam. The HbS allele frequency varies between 0.011 and 0.120, the β-thalassemia allele frequency varies between 0.005 and 0.024, and approximately 26.2% is associated with iron deficiency. (Information from Ministry of Tribal Affairs). (ACS), aseptic necrosis of bones, microinfections in the spleen, brain and kidneys, disease, paralysis and physical damage to various

organs of the body. Recent research reiterates that individuals with SCD may experience red blood cell dehydration, abnormal migration of red blood cells to the vascular endothelium, inflammatory events, and depletion of all cells in blood vessels, and abnormal nitric oxide metabolism can cause thrombotic problems and various diseases. Other problems, such as infections and hand-foot syndrome (dactylitis), occur as swelling of the hands and feet. Given the effect of infection on the spleen, the immune system of people with this disease may also be affected. Therefore, people with SCD have weak immune systems and are more prone to infections (El Ariss AB, 2016). Technologies commonly used for SCD diagnosis include high-performance liquid chromatography (HPLC), isoelectric focusing (IEF), and capillary electrophoresis (CZE).

Cell Tests

A complete blood count (CBC) is the first test used to diagnose various types of diabetes. However, heme mutations can affect hematological parameters (Greene, D.N, 2014). Peripheral blood smear (PBF) is usually performed after detecting an abnormality in the automated count and is considered an important part of the hematological evaluation. PBF examines the morphology of blood cells and evaluates any changes; this can provide important information to help identify different types of diabetes (Nwogoh, B, 1974). Another important diagnostic test is the solubility test based on HbS polymerization in the deoxygenated state. The solubility test of its content, now most used, is based on Hb-S inequality in the presence of concentrated phosphate buffer, hemolytic reagents and sodium dithionate. Electrophoresis is a chromatographic technique that is considered one of the main tests for testing Hb variants (Wajcman, H, 2011). Different pH values and environments are used to identify hemoglobin; for example, cellulose acetate electrophoresis at alkaline pH or citrate agar at acidic pH (Kotila, T, 2011). The preferred technique for this purpose is capillary electrophoresis and has been shown to separate the Hb fraction and diagnose sickle cell disease and thalassemia. Isoelectric focusing (IEF) is a high-resolution technique used to separate proteins based on their isoelectric point (pI). Hb molecules move along the pH gradient until they reach the isoelectric point where the charge is zero. Hb molecules precipitate and appear as sharp bands (Reddy, M.N, 1994). As a previous technology, HPLC has been shown to be able to separate hemoglobin due to its different interactions with the stationary phase. HPLC detects different types of heme depending on retention time and image pressure. Each hemoglobin has a specific retention time that is comparable to the retention time of known heme products. HPLC is less sensitive and reliable in monitoring patients receiving serum or hydroxyurea (Gupta, P.K, 2009).

Sickle Cell Disease: Treatment/Removal

There are three main treatment methods that change the disease, such as the use of hydroxyurea, red blood cell transplantation and hematopoietic stem cell transplantation (Ka Kassim AA, 2014). There is no treatment other than stem cell transplantation. Although there is no permanent cure, early diagnosis or universal screening remains the key to better control of the disease. Four overlapping testing phases (antenatal, perinatal, neonatal, and postneonatal) are required for effective disease management. Prenatal screening can help detect SCD ininfants with previous symptoms early in life, before birth or in the first few days of life (Arishi WA, 2021). The severity and impact of the disease varies greatly, with proper management can reduce problems, improve the lives of those affected, and improve their quality of life. The best strategy to reduce this disease is genetic education including prenatal and pregnancy counseling and information to avoid pregnancy with a child with homozygous genotype. The severity of the disease in the group is still controversial. The Government of India (GoI) and the Ministry of Tribal Affairs (MoTA) have set a target to eliminate SCD. Newborn screening is important to reduce morbidity and mortality by promoting early diagnosis and preventive treatment for individuals seeking health and harmony by the National Mission to Eliminate Sickle Cell Anemia by 2023.

CONCLUSION

There is currently no way to permanently cure this disease. However, with appropriate treatment, the severity and severity of the disease can be controlled, thereby improving the quality of life and life expectancy of the patient. This can be managed effectively by services providing medical treatment with genetic testing and counselling.

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