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Review Article**Genomic hut of Sickle Cell Anaemia disease in Indian children**

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ARTICLE INFO**ABSTRACT****Article History:**Received on 09th Sept 2017Peer Reviewed on 28th Sept 2017Revised on 14th October 2017Published on 30th October 2017**Keywords:**

Sickle cell disease, Anaemia, Erythrocytes, Haemoglobin, Vasculopathy, trait, cerebral spinal fluid test (CSF), red blood cells.

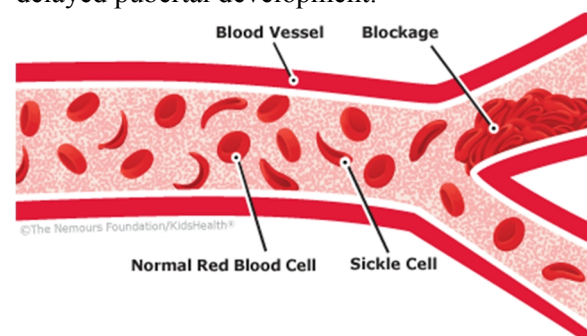
A collection of genetic red blood cell disorders refers a disease called sickle cell disease (SCD). People suffering from sickle cell anaemia have abnormal haemoglobin, which is called haemoglobin S or sickle haemoglobin in their red blood cells. In the body haemoglobin is a protein in red blood cells which carries oxygen. When the disease is delivered from parents to their children it is called genetic disease. Sickle cell anaemia is not transmissible. SCD people receives two abnormal haemoglobin genes, one from each parent. At least, one of the two abnormal genes cause a person's body to make haemoglobin S in every form of sickle cell disease. SCA is when a person has two haemoglobin S genes, haemoglobin SS. Haemoglobin S β thalassemia (thal-uh-see-me-uh) and haemoglobin SC disease are the two common forms of SCD. SCA or SCD, is a chromosomal disease of RBCs. Generally, the disc shape of RBCs gives elasticity to travel through smallest blood vessels. But the RBCs have an unusual semi-circular shape approaching a sickle which makes them tacky or sticky and inelastic and horizontal to attainment in small vessels, which blocks different parts of the body when suffering from SCD which origin discomfort and muscle injury. RBCs encompass a molecule called haemoglobin, which transfers oxygen in the whole body. A fit person haemoglobin is flat, curved, and elastic. That allows RBCs to slide along through bloodstream but SCD contains the hemoglobin's unusual form and rod like arrangement that bundle with each other which cause RBCs to convert arched and inelastic. The blood flow blocks due to odd shaped cells. This is harmful and may cause thrilling discomfort, anaemia and many indications. SCD is blood syndrome classically genetically transfers from parents. In RBCs carrying haemoglobin S, SCA causes in abnormality in theses oxygen-carrying protein and indicates to an unbending, sickle-like shape in some definite disorders. At the age of 5 to 6 months most of the complications arise of SCD.

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INTRODUCTION:

SCD is a genetic syndrome categorized by malfunctioning haemoglobin. Syndrome contains RBCs, or haemoglobin and oxygen carrying ability. The body contains haemoglobin cells which are like the letter O, round, flexible and smooth so as to travel freely and SC haemoglobin when cells becomes shape of sickle as like letter C, sticky and stiff. Through the blood vessels cells cannot move and have a tendency to group together and stop the movement of fit, usual oxygen carrying blood, cause painful and damaging complications of SCD and causes blockage in arteries and capillaries. Normally sickle cell live for approximately ten to twenty days while haemoglobin can aware about one twenty days, because of the shape and painfulness the sickle cells are destroy by the spleen. The disease-causing cells get stuck in filter and die in spleen as spleen is an organ that helps to filter the infected blood. The normal haemoglobin production is due to the 11th pair of chromosomes containing gene in all 23 pairs of chromosomes in each cell body. SCA results in the beta globin protein from single amino acid substitution. The increase in production of sickle haemoglobin (HbS). At embryonic stage, production of sickle haemoglobin (HbS) increases with balanced reduction in foetal haemoglobin (HbF) production. HbS polymerizes, causes hemolysis and shorter life span of circulating RBCs (1). The most inactivating difficulty of sickle cell anaemia is stroke. By the age of 18 years approximately some percentage of sickle cell children experience at least one symptomatic stroke. High Tran's cranial Doppler (TCD) ultrasonography velocity, anaemia, relative hypertension cerebral Vasculopathy and presence of extra cranial Vasculopathy are included in the recognized risk factors for development of stroke in kids with SCA. Children with sickle cell chronic anaemia includes largest subgroup of patients in United States, to pay for the chronic anaemia patients increase their cardiac output to maintain

oxygen delivery. Herat rate and stroke volume are the terms on which cardiac output is dependent and the increase in cardiac output is believed to be due to mainly to an increase in the stroke volume. The increased stroke volume enlarges heart (2). the abnormal sickle cell haemoglobin that polymerizes when deoxygenated is the typical view of sickle cell anaemia always concentrated on the primary genetic defect. Polymerization within RBCs deforms the shape, to develop stiff, to produce severe and prolonged tissue damages due to poor perfusion and obstruct the flow (3). For childhood development the importance of physical activity is well recognized. The symptoms in children of SCD includes limit in development of physically competitive skills and impaired cardiorespiratory responses to exercise may arise in children (4). Stroke is usually defined on the basis of clinical rather than radiological findings so terminology persists but some lesions are usually silent, in view of association with various neuropsychological abnormalities. The advance clinical care of children with SCD includes the early diagnosis, penicillin prophylaxis, folate supplementation and hydroxyurea therapy reduce morbidity and mortality. When compared with healthy peers and young adults with children with SCD are smaller than their age-matched peers and delayed pubertal development.

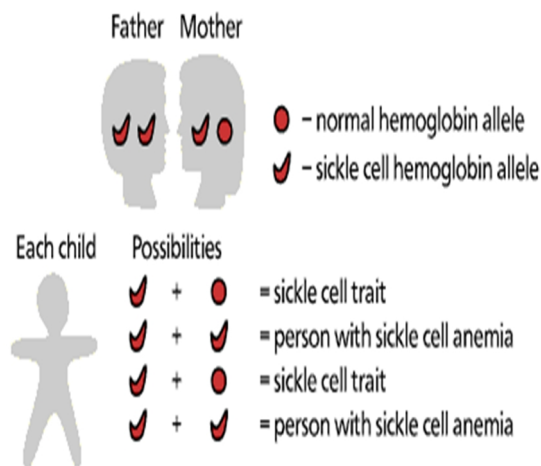


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GENETIC INHERITANCE:

The conditions which are responsible for genetic abnormal sickle haemoglobin works as heterozygous condition, the gene which could be derived from one parent only (sickle cell trait) or homozygous condition, from both parents (sickle cell anaemia). Many of the clinical features of the disease explained molecular nature of abnormalities of the cells. When the red cells comes out of solution under conditions of reduced oxygen tension the S haemo sickle cell anaemia and anesthesia globin and at last forms crystallization producing sickle shaped cells(1)

Every person has two replicas of the haemoglobin protein sequence in every cell apart from eggs and sperm in the body and get one each from mother and father. Only one of the two genes go in each egg and sperm cell. When eggs and sperms are made and when



Source: https://www.google.co.in/search?q=sickle+cell+anemia&tbs=isch&tbs=rimg:CYdgq8v_16QYIjipEAcBcKITBdl53lJRXye2XChD_GWaamg0YIVB6TLvucwj8tKFzMD8Zqn9TKHx82btXoBnXJhjoioSCakQBwFwqVMFEZ_Z3Z7e5djfKhIJ0jneUIFfj7YRdPedNTNYHcqEglcKEMZZpqaDREMyVKOKoSNNyoSCRghUHpMu5zEfFxEpTH_1wFpKhIJCPy0oXMwPxkRCNdWluR_1HWQqEgmqf1MofHzZuxEsGV_1T2ZyxWSoSCVf6gGdcMGOiERJaW_Dd0fov6&tbo=u&sa=X&ved=0ahUKEwis9PGfovTWAhUDTo8KHSvPCuYQ9C8IHw&biw=1366&bih=662&dpr=1#imgsrc=t49saob7TYoRIM:

these came together the genes baby will get therefore depend on the genes carried in parents. If one parent does not carry the sickle haemoglobin (HbAA) at all and other has sickle cell trait (HbAS) than any children will not have sickle cell anaemia. To test the type of type of haemoglobin in an unborn baby is impossible and the chances to have sickle cell trait are there is one in two chances that any given child will get one copy of HbS gene and equally likely chances (50%) that any given child will get two HbA genes and be absolutely unaffected and most importantly to test the type of haemoglobin in an unborn baby is impossible. There is a one in four (25%) chance that child could be born with sickle cell anaemia and there are one in four chances that any given child could be completely unaffected if both parents have sickle cell trait (HbAS).

MECHANISM OF ACTION:

Any abnormal haemoglobin, called haemoglobin S, causes (SCD). The small defect in the gene that directs the production of the beta globin part of haemoglobin develops problem in haemoglobin S due to which the way haemoglobin works changes and in the beta globin part of haemoglobin it causes small defect in the beta globin genes. Anyone may get sickle cell trait if haemoglobin S gene is inherited from one parent and when the normal haemoglobin gene is inherited from another parent. Sickle trait People are carriers of a defective haemoglobin S gene but only rare sickle cell trait people have complications similar to the seen in sickle cell disease people and after a child so they can pass it. If the child's other parent has SCT or another abnormal haemoglobin gene (like thalassemia, haemoglobin C, haemoglobin D, haemoglobin E) than the child has a chance of having sickle cell disease. From the substitution of a valine residue sickle cell disease results at the position 6 in the beta -subunit of haemoglobin. People with only one gene for haemoglobin S (HbS) are phenotypically normal and who inherit two HbS genes from their parents have sickle cell disease and with a few minor exceptions. Sickle

cell morphology explained when the erythrocyte deforms when deoxygenated HbS tends to polymerize non-covalently into long strands but HbS with bound oxygen does not polymerize. The erythrocytes deform as they release their oxygen in the capillaries and are trapped in the microcirculations.

SIGNS AND SYMPTOMS:

If a person has sickle cell disease, it is present at birth but until at the age of about 5 or 6 months most infants do not have any problems from the disease. Early symptoms contain:

- Hands and foot swelling.
- Tiredness or obsessiveness from anaemia
- Jaundice when yellow color of the skin when huge number of red cells hemolyzed. Symptom may be relate to problems of the disease and can differ from person to person and change over time like eye problems, heart disease, pulmonary hypertension, kidney problems, gallstones, liver complications, leg ulcers, joint complications, severe anaemia, infections, chronic pain, acute pain, , etc.
- During SCA many complications such as stroke, pulmonary hypertension, acute chest syndrome and vaso occlusive painful crisis like cough, chest pain, hypoxia, fever, infiltration on chest x rays occurs.
- HbS level increases as exercise capacity decreases in patients resulting in pulmonary dysfunction, chronic anaemia etc.(2)

DIAGNOSIS:

MATERIALS AND METHOD: - Syringes wet with heparin are used to collect the blood from venous (antecubital fossa) from patients of sickle cell anaemia. Special care is to be taken to ensure absence of air from syringe and needle. Aliquots of venous blood is to be equilibrated for 10 minutes earlier to fascination in glutaraldehyde to provide samples of maximally deoxygenated and oxygenated sickle cell anaemia erythrocytes.

- **Screening test:** To find out whether the person make sickle haemoglobin (S) or another haemoglobin and also to find out if

they carry a gene or have the trait for an abnormal haemoglobin a blood test is usually done.

- **New born screening:** on a special paper from a heel prick the blood is collected in “spots” than the haemoglobin from blood is analyzed in laboratories. To check if diagnosis is correct the blood sample is retested to be sure if the result found to be positive. Two methods are used to measure the amount of foetal haemoglobin (HbF) in RBCs of patients with (Hb SS disease): first is chemical assay of alkali resistant haemoglobin in cells distributed according to specific gravity by ultracentrifugation and second is photometry of individual cells stained for HbF and second is
- **Prenatal screening:** before the baby is born SCD is diagnosed using the liquid called amniotic fluid, or the tissue from placenta. During early 8-10 weeks into the pregnancy the test is done. The sickle haemoglobin gene are tested in the test.
- **Sickle cell test:** (HPLC) high performance liquid chromatography is used to confirm which form of haemoglobin is present (Abnormal= haemoglobin S, normal=haemoglobin A), in new-born with the disease haemoglobin F will be exclusively found.
- Simple blood test is done to prevent complications as early diagnosis and treatment and can identify SCD and SCT.

More tests used in laboratory are:

- Haemoglobin electrophoresis
- CBC count with differential and reticulocyte
- Serum electrolytes
- Haemoglobin solubility testing
- Peripheral blood smear
- Pulmonary function test
- Renal function (creatinine, BUN, urinalysis)
- CSF examination
- Blood cultures

Imaging studies: Diagnosis of sickle cell anaemia in patients include imaging studies:

- **Radiography:** patients with respiratory symptoms Chest x rays should be performed.
- **MRI:** Useful for early detection. Due to acute and chronic bone marrow infarction etc. Some neurologic examinations are also done during imaging studies by paediatric neurologist, all qualifying children underwent TCD (Tran's cranial Doppler ultrasonography) and imaging studies after a standard comprehensive examination. by imaging studies haemoglobin concentration (Hgb) and haematocrit level (HCT) is to be obtained.(3)
- **Treatment:** Stem cell transplant or bone marrow transplant is the only cure for sickle cell anaemia for people of age 16 and younger

than because the risk factors increases for people older than 16. The procedure has serious risks accompanied with this as finding a donor is difficult, and, which includes death. To prevent relieving symptoms and complications children age 2 and younger should visits to a doctor frequently. Treatments may include some medications to reduce pain and to prevent complications.

Medicines include:

- **Antibiotics:** children may begin taking antibiotics penicillin about 2 months old and continue taking until they are least 5 years old. For adults, may need to take penicillin through life.
- **Pain relieving medications:** to relieve pain during sickle cell anaemia.

Some common drugs are:

S No.	Brand Name	Generic Name	Mechanism of Action
1	Pen-vee K, Veetids	Penicillin V Potassium	Penicillin V exerts bacterial action against penicillin-sensitive microorganism during the stage of active multiplications.
2	Droxia,Hydrea	Hydroxyurea	Hydroxycarbamide decreases the production of deoxyribonucleotides
3	Alpha-E ,Alpha E mixed, Alpha-E mixed 1000, E-400 clear	Vitamin E capsules and tablets	vitamin E acts as a peroxyl radical scavenger, disabling the production of damaging free radicals in tissues
4	Glut solve, Nutrestore, SYMPT-X Glutamine	Glutamine	Functions in regulation +of gastrointestinal cell growth, function, and regeneration.

DISCUSSION:

sickle cell disease includes painful crisis which are unpredictable, recurrent, and are poorly treated manifestations and because of the advances from which the patients are benefited in both pain management and clinical understanding of the disease but by many pain specialists and sickle cell experts are not able to understand the basic principle of pain management and clinical features of the disease. (4)So, many treatments are also available in the day hospital for the pain management which includes several procedures:

- **Assessment of pain:** first is assessment of pain whether is typical or atypical. Pain relief, mood and pain intensity are included.
- **Selection of drug and dose of loading:** Patient's prior history and current assessment are important for the drug selection which includes resulting side effects, medications and patient's painful crisis.
- **Combination of drugs to increase the toxicity and efficacy ratio:** In combination with opioids antihistamines, anti-inflammatory agents and other adjuvant therapies are used.

Some degree of activity of the disease are shown by the sickle cell patients which are

demonstrated by jaundice, weakness and sometimes anaemia. This leads to crisis and severe pain which indicates exacerbation of the disease and sometimes symptoms result in increased morbidity but still unpredictable. The cause of clinical activity of the heterozygous and homozygous sickling is still in doubt but the information about haemoglobinopathies results in important contribution to medicines (5). The development of oat shaped and sickle shaped erythrocytes is characterized hematological and concluded that sickle cell anaemia is a congenital chronic hemolytic anaemia. The blood smear prepared show some cellular abnormalities which are due to excessive blood destruction and active blood formation. (6)

The results which comes out to from the surveys and the procedures is the improper awareness about the common disorder and serious disease and it is closely related to the educational level which varies from community to community. The treatment and the cure for the disease is unpredictable. Though some medicines are available for the disease but these differ according to the chronic and acute pain reliving. So setting up the requisite program for mass screening and providing people with adequate knowledge of the disease may require a significant increase in public awareness for the disease(7).

CONCLUSION:

SCD is a genetic syndrome categorized by malfunctioning haemoglobin. Syndrome contains RBCs, or haemoglobin and oxygen carrying ability. The body contains haemoglobin cells which are like the letter O, round, flexible and smooth so as to travel freely and SC haemoglobin when cells becomes shape of sickle as like letter C, sticky and stiff. Through the blood vessels cells cannot move and have a tendency to group together and stop the movement of fit, usual oxygen carrying blood, cause painful and damaging complications of SCD and causes blockage in arteries and capillaries. Normally sickle cell live for approximately ten to twenty days while

haemoglobin can aware about one twenty days, because of the shape and painfulness the sickle cells are destroy by the spleen. The disease-causing cells get stuck in filter and die in spleen as spleen is an organ that helps to filter the infected blood. The normal haemoglobin production is due to the 11th pair of chromosomes containing gene in all 23 pairs of chromosomes in each cell body. The conditions which are responsible for genetic abnormal sickle haemoglobin works as the action of a gene which could be derived from both parents to produce the homozygous condition (sickle cell anaemia) or from one parent only to produce the heterozygous condition (sickle cell trait) or from). Many of the clinical features of the disease are explained by molecular nature of abnormalities of the cells. When the red cells come out of solution under conditions of reduced oxygen tension the S haemo sickle cell anaemia and anesthesia globin and at last forms crystallization producing sickle shaped cells. When the normal haemoglobin gene is inherited from another parent. Sickle trait People are carriers of a defective haemoglobin S gene but only rare sickle cell trait people have complications similar to the seen in sickle cell disease people and after a child so they can pass it. If the child's other parent has SCT or another abnormal haemoglobin gene (like thalassemia, haemoglobin C, haemoglobin D, haemoglobin E) than the child has a chance of having sickle cell disease. From the substitution of a valine residue sickle cell disease results at the position 6 in the beta -subunit of haemoglobin. People with only one gene for haemoglobin S (HbS) are phenotypically normal and who inherit two HbS genes from their parents have sickle cell disease and with a few minor exceptions. The diagnosis involves some test which include blood test, fluid test and haemoglobin electrophoresis, CBC with differential and reticulocyte, serum electrolyte, cerebrospinal fluid test, blood culture etc. To prevent complications and relieving symptoms babies and children age 2 and younger with sickle cell anaemia should frequent visits to a doctor. Treatments may include medications to reduce

pain and prevent complications and blood transfusion etc. for the treatment many antibiotics are also involved which may help in relieving pain or given to the infants so as to cure the disease to become severe.

The results which comes out to from the surveys and the procedures is the improper awareness about the common disorder and serious disease and it is closely related to the educational level which varies from community to community. The treatment and the cure for the disease is unpredictable. The screening programs are also available for the disease but the only and most important aspects of any screening program is the measure of the attention devoted to those patients found to have the disease or the trait. So that the people may get aware and able to start their medications so as to early cure and treat for the sickle cell disease.

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