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# PREVENTION AND CONTROL PROGRAM

For

Government of Maharashtra

(Directorate of Medical Education & Research)

(Draft - June 2008)

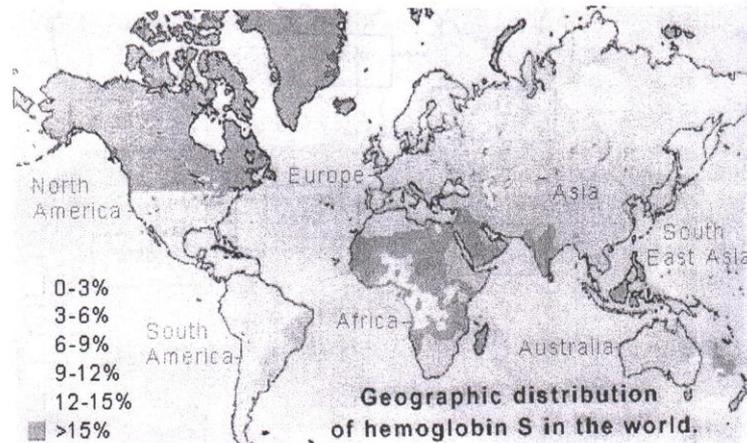
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# Sickle Cell Anemia

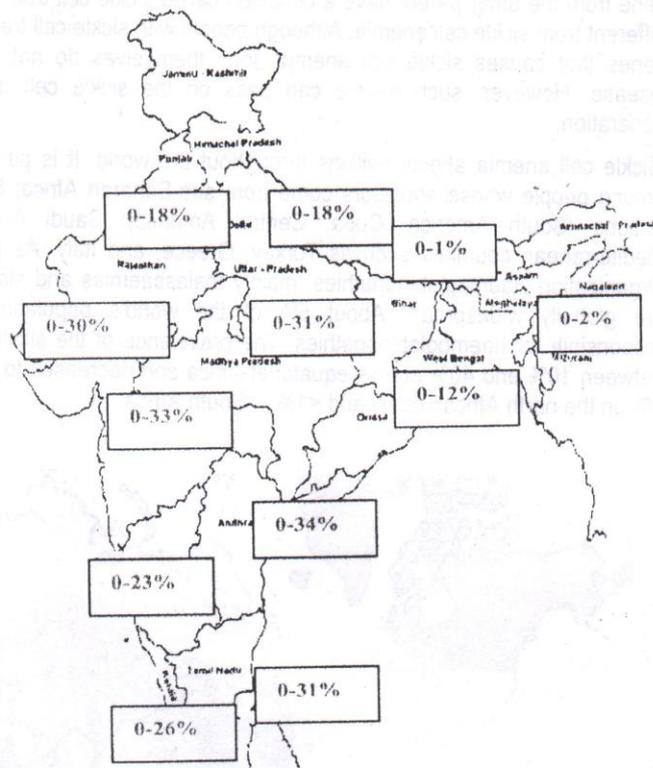
## I. INTRODUCTION

- 1.1 Sickle cell anemia is a serious condition in which the red blood cells can become sickle-shaped (that is, shaped like a "C"). Normal red blood cells are smooth and round like a doughnut without a hole. They move easily through blood vessels to carry oxygen to all parts of the body. Sickle-shaped cells do not move easily through blood; they are stiff and sticky, and tend to form clumps and get stuck in blood vessels. The clumps of sickle cells block blood flow in the blood vessels to the limbs and organs. Blocked blood vessels can cause pain, serious infections and organ damage.
- 1.2 Sickle Cell Anemia is known all over the world by various names namely Hemoglobin SS disease, Hemoglobin S disease, HbS Disease, Sickle Cell Disorders, Sickling Disorder due to Hemoglobin S or SCD (Sickle Cell Disease)
- 1.3 Sickle cell anemia is an inherited, lifelong condition. People who have sickle cell anemia are born with it. They inherit two copies of the sickle cell gene, one from each parent. People who inherit a sickle cell gene from one parent and a normal gene from the other parent have a condition called sickle cell trait. Sickle cell trait is different from sickle cell anemia. Although people with sickle cell trait have one of the genes that causes sickle cell anemia, they themselves do not suffer from this disease. However, such people can pass on the sickle cell gene to the next generation.
- 1.4 Sickle cell anemia affects millions throughout the world. It is particularly common among people whose ancestors come from sub-Saharan Africa; Spanish-speaking regions (South America, Cuba, Central America); Saudi Arabia; India; and Mediterranean countries such as Turkey, Greece, and Italy. As per World Health Organization Haemoglobinopathies, mainly thalassaemias and sickle-cell anaemia, are globally widespread. About 5% of the world's population carries genes responsible for haemoglobinopathies. The prevalence of the sickle-cell trait ranges between 10% and 40% across equatorial Africa and decreases to between 1% and 2% on the north African coast and <1% in South Africa.

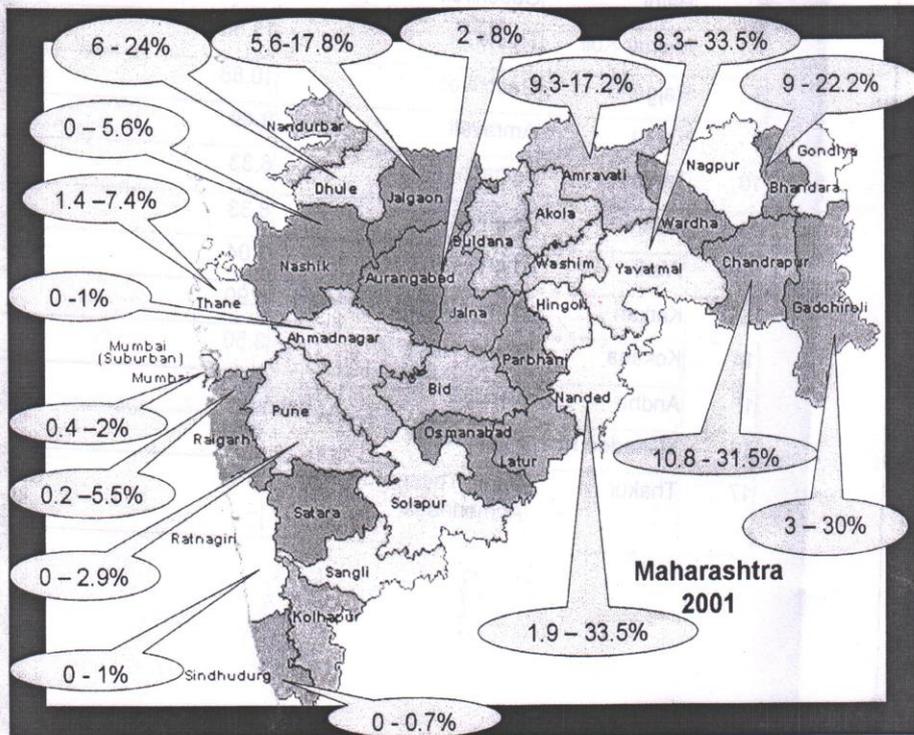


1.5 The prevalence of the disease is determined by the presence of the sickle cell gene, the carrier state or sickle cell trait. Estimates from India indicate that the sickle cell trait occurs in 10-30% of many, predominantly tribal population. Projections from the gene frequency suggest that there may be between 5,00,000 and 10,00,000 cases of disease in India. In India Sickle Cell Anemia is the second most common hemoglobinopathy next to thalassemia. In 1952, sickle haemoglobin was first discovered by Lahmann and Cutbush among the tribals of Nilgiri Hills of Southern India. Almost at the same time, Dunlop and Muzumdar reported the presence of the disease in Assam. In 1953, Buchi confirmed presence of disease in Veddoids of South India. In 1955, Sukumaran found it in Western-India. Later, subsequent studies conducted by various workers reported its high frequencies throughout Central India and parts of Southern India. The highest frequency of sickle cell gene is reported in Orissa followed by Assam, Madhya Pradesh, Uttar Pradesh, Tamil Nadu, Maharashtra and Gujarat

### Distribution of sickle cell gene in India



1.6 In Maharashtra Sickle cell disease is a major genetic disorder amongst Scheduled Caste (SC), Scheduled Tribe (ST), and Other Backward Communities (OBC) population groups of Maharashtra. Studies carried out from different institutions indicate that the overall prevalence of sickle cell disorder in different tribal populations is 10% for carrier state and 0.5% for the sufferer. The total tribal population from the State of Maharashtra as per the recent Govt. record is 90 lakhs at the end of the 20th century. Based on this number, the expected carriers of sickle cell would be 9 lakhs and expected number of sickle cell homozygotes would be 45,000. The prevalence is very high among the Bhil and Pawara tribal groups from the Nandurbar District and the Madia, Pardhan, Otkar and Gond from the Gadchiroli District. It is estimated that there are more than 10,000 sickle cell patients in the Nandurbar District itself. The Gadchiroli District is expected to have more than 5,000.



(Prevalence of Sickle Cell Disorder in Maharashtra in tribal population)

Distribution of sickle cell trait among different tribal groups of Maharashtra (Kate<sup>5</sup>)

Sr. No	Tribal Group	District	Sickle Cell Carriers (%)
1	Otkar	Gadchiroli	35
2	Pardhan	Nanded, Yeotmal	33.7
3	Pawara	Dhule, Jalgaon	25.18
4	Madia, Gond	Gadchiroli, Yeotmal	20.8
5	Bhil	Nandurbar	20.6
6	Halbi	Gadchiroli	13.93
7	Malhar Koli	Thane	13.88
8	Rajgond	Gadchiroli	10.88
9	Korku	Amravati	9.49
10	Tandvi	Jalgaon	8.33
11	Kolam	Yeotmal	8.33
12	Wari	Thane	8.04
13	Katkari	Pune, Raigad, Ratnagiri	5.90
14	Kokana	Dhule, Nasik	3.50
15	Andha	Nanded	1.97
16	Mahadeo Koli	Pune, Nasik	0.81
17	Thakur	Pune, Thane, Raigad, Ahmednagar	0.00

## II. Sickle Cell Anemia

- 2.1 Sickle cell anemia is an inherited condition. People with sickle cell anemia inherit two copies of the sickle cell gene, one from each parent. The sickle cell gene makes abnormal hemoglobin. Hemoglobin is the protein inside red blood cells that carries oxygen to all parts of the body and gives blood its red colour. In sickle cell anemia, the abnormal hemoglobin sticks together when it gives up its oxygen to the tissues. These clumps are like liquid crystals that cause red blood cells to become stiff and shaped like a sickle, or "C." It takes two copies of the sickle cell gene for the body to make the abnormal hemoglobin found in sickle cell anemia.
- 2.2 Sickle Cell Trait: People who inherit only one copy of the sickle cell gene (from one parent) will not have sickle cell anemia. They will have sickle cell trait. People who have sickle cell trait generally have no symptoms and lead normal lives. However, like people with sickle cell anemia, however, they can pass the sickle cell gene on to their children.
- 2.3 The signs and symptoms of sickle cell anemia are different in each person. Some people have mild symptoms others have very severe symptoms and are often hospitalized for treatment. Although sickle cell anemia is present at birth, many infants do not show any signs until after four months of age. The most common signs and symptoms of sickle cell anemia are linked to anemia and pain. There may be signs and symptoms linked to special conditions of patient. The general signs and symptoms of anemia like fatigue, pallor, jaundice and dyspnea may be present, however, sudden episodes of pain throughout the body are a common symptom of sickle cell anemia and are often referred to as "sickle cell crises. Almost all people with sickle cell anemia have painful crises at some point in their lives. Some have a crisis less than once a year. Others may have fifteen or more crises in a year. The most common sites affected by sickle cell crises are the bones, lungs, abdomen, and joints. The blocked blood flow can cause pain and organ damage.
- 2.4 Some of the complications of Sickle Cell Anemia are Hand-Foot Syndrome, Splenic (Sequestration) Crisis, Infections like Pneumonia, Meningitis, influenza, and hepatitis, Acute Chest Syndrome, Delayed Growth and Puberty in Children, Stroke, Eye Problems, Priapism, Gallstones, Ulcers on the Legs, Pulmonary Arterial Hypertension (High Blood Pressure) and Multiple Organ Failure.
- 2.5 Early diagnosis of sickle cell anemia is very important so that children who have the condition can get timely treatment. The following tests are useful in diagnosis
- i) **Screening tests:** These are simple easy to carry out tests used to screen the population for the presence of sickle cell disease. Solubility test and Sickling test are two such screening tests. In solubility test a chemical is added to the patient's blood sample that reduces the amount of oxygen it carries. The reduced amount of oxygen will cause S-related polymers to form. The sickle cell solubility test relies on the relative insolubility of Hb S in concentrated phosphate buffers compared to Hb A and other Hb variants. Hb S precipitates causing a cloudy solution. This test detects the presence of hemoglobin S. It should not be performed on infants until they are about 6 months old because babies with sickle cell will not produce significant amounts of hemoglobin S until several months after birth. Solubility testing methods also fail to detect sickle hemoglobin in persons with severe anemia. In Sickling test on addition of a reducing substance (metabisulfite) the red blood cells undergo sickling.
  - ii) **Confirmatory tests:** Patients tested positive by the screening test have to undergo confirmatory tests like Hemoglobin electrophoresis, isoelectric focusing.

high-performance liquid chromatography or DNA analysis. If both parents are accessible, studies of parental blood can aid in the diagnosis of sickle cell disease in the child. DNA analysis provides the most accurate diagnosis in patients of any age, but it is still relatively expensive.

**iii) Prenatal Diagnosis** Prenatal testing refers to tests that are done during pregnancy to either screen or diagnose a case.

**1<sup>st</sup> trimester:** Chorion villus sampling and DNA analysis using reverse dot blot hybridization or restriction enzyme digestion

**2<sup>nd</sup> trimester:** Cordocentesis and fetal blood analyses by automated HPLC

**iv) Neonatal Diagnosis**

Infants from high-risk groups can be screened by hemoglobin electrophoresis prior to two months of age those found positive to be confirmed by Iso-electric focusing (IEF), High Performance Liquid Chromatography (HPLC) and/or DNA-based methods.

2.6 Effective treatments are available to help relieve the symptoms and complications of sickle cell anemia, but in most cases there's no cure. Bone marrow transplants and gene therapy may offer a cure in a small number of cases. People who have sickle cell anemia need regular medical care. The goals of treating sickle cell anemia are to relieve pain; prevent infections, eye damage, and strokes; and control complications if they occur. The treatments include medicine, blood transfusions, and specific treatment for complications.

2.7 Treatment comprises of Treating pain with Heating pads and Acute pain crises with Analgesics like Acetaminophen Nonsteroidal anti-inflammatory drugs (NSAIDs) Narcotics - meperidine, morphine, oxycodone etc; In addition Fluids to prevent dehydration, Hydroxyurea to prevent & reduce the number of painful crises and blood transfusions.

2.8 Treating Other Complications like Acute chest syndrome, Leg ulcers, Gallstones Priapism etc;

2.9 New treatment modalities like bone marrow transplant and gene therapy

2.10 New Medicines like Butyric acid (a food additive that may increase normal hemoglobin in the blood), Clotrimazole (an antifungal agent that helps prevent the loss of water from red blood cell and can keep the cell from turning into a sickle cell) and Nitric oxide (this may make sickle cells less sticky and keep blood vessels open).

### III. PREVENTION

**3.1** Sickle cell anemia is an inherited condition. Children who inherit the genes for sickle cell anemia can't prevent developing the condition, although they can take steps to reduce complications. People who are in groups that are at high risk for sickle cell anemia and who are planning to have children should be counseled. With good health care, many people with sickle cell anemia can live productive lives, have reasonably good health much of the time, and live longer today than in the past. Many people who have sickle cell anemia now live into their forties or fifties, or longer.

**3.2** Preventing Infections. Infection is a major complication of sickle cell anemia. Pneumonia is the leading cause of death in children with the condition. Other infections common in people with sickle cell anemia include meningitis, influenza, and hepatitis. To prevent infections in babies and young children, antibiotics like penicillin may begin as early as two months of age and continue until the child is at least five years old. In addition the child has to be administered vaccinations for pneumonia, meningitis, influenza, and hepatitis.

**3.3** Affected individuals should take care of their health and maintain healthy lifestyle habits. These include:

- Eating healthy. Folic acid is recommended daily to help the body make new red blood cells.
- Drinking at least 8 glasses of water every day, especially in warm weather.
- Exercising regularly and drinking lots of fluids when exercising.
- Getting enough sleep and rest.
- Limiting the amount of alcohol
- Quitting smoking.

**3.4** Along with healthy lifestyle habits, there are some things that can help prevent a sickle cell crisis:

- Getting medical help when there are any signs of an infection, such as a fever or trouble breathing. Avoiding decongestants, such as pseudoephedrine, that can constrict blood vessels.
- Avoid exposures to extremes of heat and cold avoiding swimming in cold water or climbing high altitudes without extra oxygen.
- Avoiding strenuous physical labor
- Avoiding travel in airplanes where the cabin isn't pressurized
- Regular medical checkups and treatment.
- Learning to recognize the symptoms of complications that are commonly encountered in sickle cell patients.
- Receiving vaccinations to prevent infections.
- Pre marriage and marriage counseling before conceiving

#### IV. SUMMARY

- Sickle cell anemia is a serious condition in which the red blood cells can become sickle-shaped (that is, shaped like a "C").
- Sickle-shaped cells don't move easily through the blood. They're stiff and sticky and tend to form clumps and get stuck in blood vessels. The clumps of sickle cells block blood flow in the blood vessels, causing pain, serious infections, and organ damage.
- Sickle cell anemia is an inherited, lifelong condition. People who have sickle cell anemia are born with it. They inherit two copies of the sickle cell gene, one from each parent.
- People who inherit a sickle cell gene from one parent and a normal gene from the other parent have a condition called sickle cell trait. People with sickle cell trait don't have the condition, but they can pass the sickle cell gene on to their children.
- Sickle cell anemia affects millions of people worldwide. It's most common in people whose families come from Africa, South or Central America (especially Panama), Caribbean islands, Mediterranean countries (such as Turkey, Greece, and Italy), India, and Saudi Arabia.
- The signs and symptoms of sickle cell anemia are different in each person. Some people have mild symptoms. Others have very severe symptoms and are often hospitalized for treatment.
- The most common signs and symptoms of sickle cell anemia are linked to anemia and pain (also referred to as a "sickle cell crisis").
- Infection is a major complication of sickle cell anemia. Pneumonia, in particular, can be a life-threatening complication in children with sickle cell anemia. Routine treatment with penicillin and vaccinations are used to prevent infection in children.
- Strokes are a major complication for children with sickle cell anemia. Routine screening and early treatment can prevent strokes.
- Early diagnosis of sickle cell anemia is very important so that children who have the condition can get proper treatment.
- Effective treatments are available to help relieve the symptoms and complications of sickle cell anemia, but in most cases there's no cure. (Some researchers believe that bone marrow transplants may offer a cure in a small number of cases.)
- Sickle cell anemia is treated with medicines, blood transfusions, and other treatments specific to certain complications.
- Researchers are working to develop new treatments for sickle cell anemia, including gene therapy and safer and more effective bone marrow transplants.

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