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Department of Health Research
Ministry of Health and Family Welfare, Government of India

INDIAN COUNCIL OF MEDICAL RESEARCH
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Standard Treatment Workflow (STW)

SICKLE CELL DISEASE

ICD-10-D57

GENERAL INTRODUCTION

- Hemolytic anemia, where RBCs sickle under hypoxia or stress. Sickling and inflammation lead to vaso-occlusive crisis (VOC) and organ damage
- Autosomal recessive - mutations in the β-globin gene
- ~88% of sickle homozygous cases in Asia are Indians

SUBTYPES

Carriers/ heterozygous (HbAS)	Disease/ sufferer/ homozygous (HbSS)	Other symptomatic genetic variants
Have only one disease allele, usually asymptomatic	Have both defective alleles, usually symptomatic	HbS-β thalassemia, HbSD-Punjab disease, HbSE disease etc.

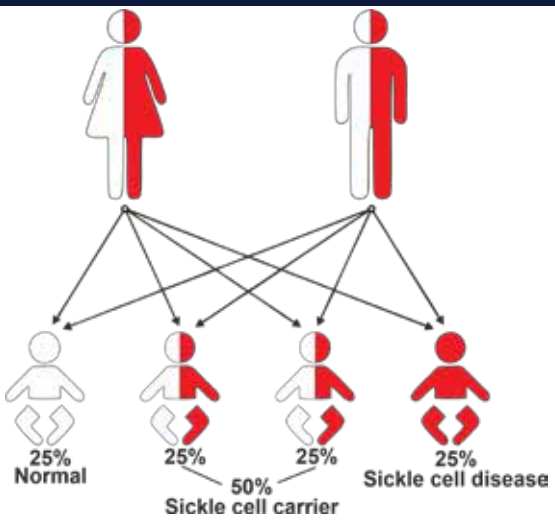
MANIFESTATIONS OF VOC

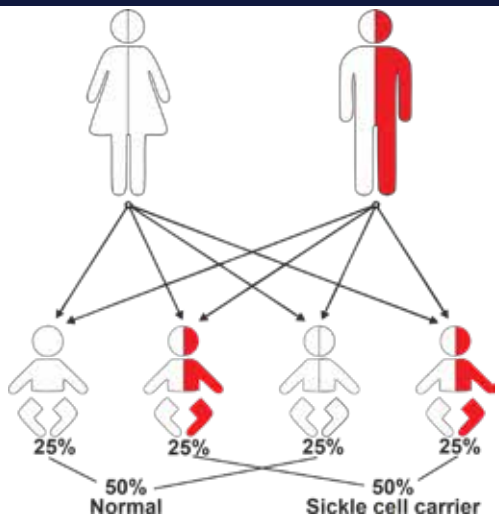
- Experienced as pain, or swelling
- Each VOC can lead to long lasting problems and end-organ damage
- Typical sites - hands and feet, limbs, abdominal viscera, ribs, sternum etc.
- The crisis is usually precipitated by fever, strenuous exercise, dehydration, drenching in rain, surgery, infection etc.

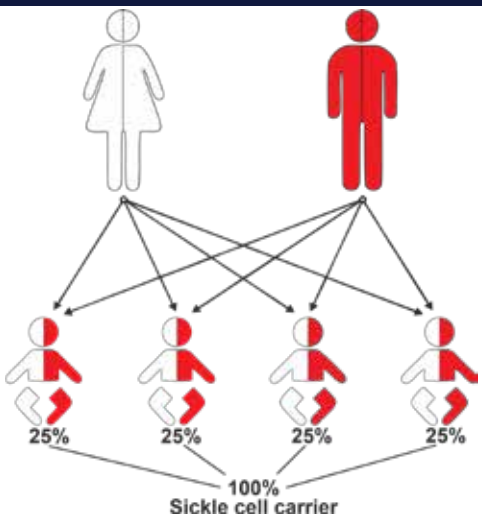
THIS FAMILY TREE SHOWS THROUGH MENDELIAN TRANSMISSION - THE RISK OF HAVING AFFECTED CHILDREN ACROSS GENERATION IN PARENTS WITH SCD - HETEROZYGOUS AND HOMOZYGOUS.

LEGEND

- Half red color – one affected allele - carrier (HbAS)
- Full red color – two affected alleles - homozygous/ diseased (HbSS)
- No red color – both alleles normal







CLINICAL MANIFESTATIONS OF SCD

- Common presentations - Pain, anemia, icterus, increased risk of infection
- Acute morbidity/ events - Splenic sequestration, fatigue, acute chest syndrome, priapism
- Long term complications - End organ damage, hepatopathy, chronic kidney disease, hypersplenism, avascular necrosis of femur, osteomyelitis, pulmonary hypertension, cholelithiasis, functional disability, retinopathy, foot ulcers- refer to a higher center for adequate management

Target group to be screened	Tests / remarks
Antenatal Mothers or pre-pregnancy planning	• CBC all women in first trimester • In endemic pockets/ high risk population: solubility test/ POC tests for sickle cell • Or HPLC/ electrophoresis, if available » If mother is a sickle cell carrier/ disease, » Then testing of father is mandatory, » Ideally by HPLC, if not available refer to higher center » If father tests positive, counselling and pre-natal testing should be performed (at centers with necessary facilities) to prevent risk of birth of affected newborn
Newborn	• POC tests to initiate penicillin prophylaxis in baby and enrolling vaccination program • HPLC and electrophoresis, if available or at later date
Population screening/ patient of any age	• In endemic pockets/ high risk population: solubility test/ POC tests for sickle cell

GENERAL PRINCIPALS OF MANAGEMENT

- Carriers are usually asymptomatic and need no treatment
- The goal of management is to improve quality of life and life expectancy of the affected individuals
- Episodes of fever have to be dealt with early and aggressively
- Early and aggressive management of pain should be advocated, since pain may be indicative of microvascular organ damage. Pain management using paracetamol, diclofenac or tramadol. For severe pain, refer to higher centre
- Malaria in SCD patients will be present with same frequency as endemic prevalence
- Evaluate for anaemia. Iron supplements for anemia to be used cautiously (low dose - not more than 3 months). Other nutritional causes (Vit B12, and Folic acid deficiency) and infectious causes (worm infestations) to be evaluated
- Prophylaxis for infections– penicillin, immunizations and folic acid supplement, disease modifying agents like hydroxyurea (HU) and blood transfusions have specific indications
- Acute morbidity events occur over the lifetime and require management, regular monitoring may help to reduce severity of complications
- Only curative therapy is hematopoietic stem cell transplantation. This is recommended and beneficial in a small subset of patients not responding to HU or newer disease modifying agents

PROPHYLAXIS FOR ALL SCD PATIENTS

New born HbSS till 5 years of age	Penicillin prophylaxis- 65mg BD, less than 12 months 125 mg BD till 2 years , then 250mg BD till 5 years lifelong if post splenectomy
To prevent megaloblastic crises	Folic acid- less than 1 year of age, 2.5 mg daily > 1 year of age, 5 mg daily
Common recommended vaccinations	Pneumococcal vaccine Meningococcal vaccine H-influenza vaccine Typhoid vaccine Influenza vaccine COVID 19 vaccine

HOW TO PRESCRIBE HYDROXYUREA

Indications for HU	Baseline Investigations	Dosing	Toxicity
• Above 2 years of Age • All children more than 9 months of age may be offered	• Complete physical Examination • CBC • Liver function test • Renal function • Pregnancy test for relevant population	• Infants and Children: 10-15 mg/kg/day • Adolescents: 15mg/kg/day • Dose escalation by 5 mg/kg; 2-3 months only in definite indications • CBC monitoring 1-3 months when starting the medicine or if dose change	• Common dose dependent toxicity: anaemia, nausea, diarrhoea, gastritis, may require discontinuat - ion • Nail/ skin hyperpigme - ntation • Long term toxicity: Mucositis or leg ulcers

Red Flag for hospitalization or referral to higher centre

- Acute illness requiring immediate medical care, including emergencies
- Persistent Temperature >38 ^{0}C
- Pain inadequately relieved by home measures
- Significant respiratory symptoms (cough, shortness of breath, chest pain) or hypoxia
- Abdominal pain, distention, acute enlargement of spleen
- Any neurological signs or symptoms
- Significant increase in pallor, fatigue, lethargy
- Significant vomiting and diarrhoea

EDUCATION AND GENETIC COUNSELING

- **Medical disease counselling -** Explain the clinical presentation, severity, consequences of the disease. Importance of early diagnosis by newborn screening and comprehensive care. Teach patients and parents –avoid infections, be adequately hydrated, balanced nutrition, avoid over exercise, 9avoid extreme temperatures, importance of penicillin prophylaxis, need for regular clinical follow up of patients
- **Genetic counselling -** Explain carrier state and risk of having an affected child. Document family history, consanguinity, draw a pedigree chart, explain the inheritance pattern and risk of recurrence
- **Preconception care counselling -** for at-risk couples by following recommended practices. Give options and referrals
- **Pre and post test support to the family -** while making decisions and eliminating irrational fears, stigmatization, maintaining confidentiality
- **Cascade screening -** Emphasize the need for screening of extended family members

EARLY AND AGGRESSIVE MANAGEMENT OF PAIN AND INFECTIONS WILL HELP IMPROVE LONG TERM OUTCOME