# Sickle cell disorders

## *Executive summary*

## Introduction

Haemoglobin (Hb) is a tetrameric protein composed of four subunits. In the foetus, the predominant Hb is HbF (which has 2 alpha and 2 gamma subunits). This is replaced in the postnatal period by HbA (which has 2 alpha and 2 beta subunits) and HbA2 (2 alpha and 2 delta subunits).

In sickle cell disease, an individual inherits 2 abnormal beta subunits, at least one of which is HbS. This produces red blood cells which are prone to sickling and cause a range of symptoms and pathology.

The common sickle cell syndromes are: HbSS disease, HbSC disease, HbS-beta thalassaemia and other rare variants. The inheritance of SS disease follows simple Mendelian principles.

## Target users

* Doctors
* Nurses

## Target area of use

* Ward
* Outpatient department

## Key areas of focus / New additions / Changes

This guideline outlines the initial diagnosis and management of sickle cell disease and its complications.

## Limitations

Exchange transfusion and modern preventative treatments such as hydroxyurea are not available in the Gambia.

## Presenting symptoms and signs

The most common signs and symptoms are linked to anaemia. As a result, they may feel tired or weak. Fatigue is one of the most common symptoms of sickle cell anaemia.

* Non-specific symptoms:
  + Fatigue
  + Headaches
  + Dizziness
  + Fever
* Pain in any part of the body
* Symptoms of specific syndromes:
* Shortness of breath
* Cough
* Abdominal distension
* Swelling of the hands or feet
* Leg ulcers

## Examination findings

The early signs include: pallor, jaundice, hepato-splenomegaly (signs of visceral sequestration) and hand-foot syndrome (dactylitis).

Signs consistent with important complications include:

* Tachycardia, tachypnoea and hypotension (signs of sepsis)
* Signs of heart failure and murmur due to anaemia
* Respiratory distress (acute chest syndrome)
* Bone pain consistent with vaso-occlusive crisis or osteomyelitis
* Priapism
* Haematuria
* Evidence of stroke
* Leg ulcers
* Frontal bossing and protrusion of upper teeth (gnathopathy)

## Differential diagnoses

* Rheumatic fever
* Rheumatoid arthritis
* Osteomyelitis
* Leukaemia
* Splenic abscess
* Hepatitis
* Ischaemic colitis
* Peptic ulcer.

## Investigations

* Blood Tests:
  + Hb genotype (sickle test has very low specificity and sensitivity and is not useful)
  + FBC & reticulocytes( Reduced Hb, elevated WCC, elevated Platelets, increased retics)
  + Group and save
* Blood film or RDT for malaria parasites (sickled cells, poikilocytes and target cells)
* Microbiological screen: Urine dipstick & culture, blood culture
* Radiology:
  + Chest x-ray if indicated (i.e. symptoms/signs)
  + X-ray of the hands: initially not informative but later shows evidence of destruction and repair of bones

## Management in OPD

### Antibiotics:

Patients who have previously been admitted to hospital with a serious infection should be treated with prophylactic penicillin V 7.5 mg/kg up to 500 mg BD.

### Folic acid:

From 1 month to 3 years of age, give 2.5 mg OD. Above 3 years of age give, 5 mg OD.

### Anti-malarials:

Patients should receive anti-malarial prophylaxis during the transmission season. This should usually be started as soon as the first rain has occurred (and not before) and should continue until the end of the calendar year. Give mefloquine (5-10 mg/kg up to 250 mg once per week).

### Appointments

Children with sickle cell disease are seen 3 monthly until 2 years of age and six-monthly thereafter, unless there are medical, educational or psychosocial concerns in which case they should be seen more frequently. If patients are stable, in Fajara, they should be referred on to another health facility for ongoing care.

Children who have frequent crises have been shown to have better outcomes if their parents bring them for medical care sooner when they deteriorate. Teach carers about the importance of taking pain and fevers seriously. Studies have shown that parents can be taught to recognize splenomegaly, which is an indication to present to the clinic.

## Management on the ward

Management is supportive unless there are complications or indications for exchange transfusion. (This is not routinely offered and must be discussed with a consultant.)

General management includes:

* Reassurance that the patient’s pain will be relieved as soon as possible
* Massage and distraction techniques may help some children
* Warmth
* Establishing a position of maximum comfort
* Hyperhydration (see below)
* Oxygen supplementation when necessary
* Establish IV access as soon as possible
* Identification and treatment of infection
* Regular observations and reassessment

### Fluids (Sodium chloride 0.9%)

Aim to give 1.5 times as much fluid as usual:

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| **Body weight (kg)** | **Fluids (mL/kg/day)** |
| Up to 10 kg | 150 mL/kg/day |
| 11 - 20 kg | 1500 mL + 75 mL/kg/day for each kilo over 10 kg |
| >20 kg | 2250 mL + 30 mL/kg/day for each 1 kg body weight over 20kg |

### Analgesia

An analgesic ladder is used according to the severity of pain and a pain tool must always be used to monitor effectiveness of pain relief.

Give paracetamol (15 mg/kg up to 1 g QDS) or ibuprofen (5 mg/kg up to 400 mg TDS) as a single agent of pain relief if not already given.

If pain persists, give paracetamol and ibuprofen together.

If pain persists, continue paracetamol and ibuprofen and add:

* Codeine phosphate (0.5-1.0 mg/kg up to 30 mg TDS) for rapid oral opiate pain relief.
* If injectable pain relief required: SC Morphine (begin with 0.1-0.2 mg/kg up to 2.5 mg and titrate until pain is controlled).
* If the patient requires regular on-going opiate pain relief, Morphine Slow-release Tablets (MST) may be used in place of codeine phosphate. To find the equivalent dose, divide total daily dose of codeine by 8-10 and give half this amount as MST BD).

## Management of complications

**Veno-occlusive crisis:** Presents with bone or body pain. Occurs when hypoxia, infection, dehydration or pregnancy trigger sickling which causes capillary blockage. This results in local ischaemia of tissues. In infants and toddlers, it often affects the hand and feet and presents as dactylitis (which is a poor prognostic factor). If the spleen is involved, it may suddenly enlarge and is very painful. This is also a poor prognostic factor. Treatment is with pain relief and hyperhydration. If there is evidence of infection, this should be treated.

**Infection**: Occurs as a complication of a veno-occlusive crisis or secondary to asplenism. Patients are at increased risk of sepsis from capsulated bacteria including *pneumococcus*, *haemophilus influenzae* and *salmonella* spp. Patients presenting with infections severe enough to require hospital admission should be treated with the usual antibiotics indicated for the suspected site of infection. The exception to this is osteomyelitis, which should be treated with chloramphenicol 25 mg/kg up to 500 mg QDS for 2 weeks. Also, ensure child is fully vaccinated as this helps with infection from some of the encapsulated bacteria listed above.

**Stroke:** This is a complication of veno-occlusive crisis affecting the brain. Ten percent (10%) of sickle cell patients will have a stroke before the age of 20 years and those who have had one stroke have a 60% chance of having a second stroke. Patients with an acute stroke have a better outcome if they receive blood transfusion to keep their Hb above 10 g/dl and oxygen to keep their saturations above 95%. They should then continue to receive regular transfusions to keep their Hb at 10 g/dl. This should ideally be done by exchange transfusion, but this is not available in our setting.

**Acute chest syndrome:** This is a complication of veno-occlusive crisis affecting the lungs. This is commonly associated with secondary respiratory infection. The mortality rate is 10% even in the best centres. The patient should be treated with oxygen, salbutamol nebulisers and benzyl penicillin 500,000 units/kg up to 2 megaunits QDS and chloramphenicol 25 mg/kg up to 500 mg QDS. Transfuse if the Hb is below 10 g/dl.

**Renal failure:** will occur in one third of patients over their lifetime. This is due to recurrent renal ischaemia. Patients with sickle cell disease who are admitted must be adequately hydrated as above.

**Complications of pregnancy:** occur when the placenta becomes ischaemic during a crisis. This presents with spontaneous abortion, placental abruption and premature labour. Pregnant sickle cell patients require specialised obstetric care. Early referral to the O&G unit of EFSTH is thus necessary.

**Priapism:** occurs when sickling affects the penis and is very painful. It should be treated with adequate pain relief and hyperhydration. If there is no rapid relief, blood must be aspirated from the penis with a needle. Referral to the urologist is necessary at this point.

## Key Issues for Nursing care

* Timely assessment of patients.
* Advocate for rapid and effective treatment of pain.
* Develop trusting relationship with patient and family.
* Educate patients to use a pro-active approach in pain management.

## References

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Nelson text book of paediatrics

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