SICKLE

WHO SICKLE Package of Interventions for Sickle Cell Disease Management

Insight into Sickle Cell Disease

Module 2

World Health Organization
African Region

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Noncommunicable Diseases (UCN) Cluster
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WHO SICKLE package of interventions for sickle-cell disease management: insight into sickle cell disease: Module 2

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Contents

V Acknowledgements

01 Background

03 Understanding sickle-cell disease

Figures

05 **Fig. 1** Inheritance pattern of sickle-cell anaemia

06 **Fig. 2** Diagram of body showing SCD clinical features

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UNDER ARMOUR

1. Background

1.1 Rationale

Sickle-cell disease (SCD) is the most common genetic disease, affecting 0.5–2% of newborns in Africa, but it is neglected despite its seriousness. Common symptoms include chronic pain, anaemia and jaundice. Inadequate training for health care professionals and financial constraints, notably the lack of access to hydroxyurea, are the main challenges. Inequality and injustice in terms of provision of care are often cited to explain why people from low-income settings cannot benefit from progress. Sickle-cell disease is a common enemy to be fought by information, early detection and sustained efforts to provide optimal and excellent care for basically deprived populations.

This guide is meant to serve as a reference document that emphasizes the practical dimension of the disease in the African context. This will be achieved by identifying the existing clinical research products on the disease and proven treatments, which should be applied to this type of management.

The production of a guide for the effective and efficient management of African patients living with sickle-cell disease, pooling of skills and energies for harmonized, state-of-the-art patient management and care practices, knowledge sharing, research from different countries, regions, African subregions, and elsewhere, all come at just the right time.

1.2 Scope and use of the guide

This guide will serve as a reference for health care professionals in the prevention and management of sickle-cell disease. Hard copy and electronic versions of the guide will be presented to ministries of health and health facilities for consultation by doctors, nurses, midwives, laboratory technicians, anaesthetists, surgeons, and paediatricians. The annexes can be presented as individual posters in specific health centres and basic health centres.

1.3 Target audience

This guide is designed for all health care workers/health professionals, medical and paramedical personnel working in health facilities ranging from basic community health centres to centres of excellence and hospitals at all levels, as well as for programme managers and all stakeholders.

1.4 Objectives of the guide

The fundamental objective is to reduce mortality among patients with SCD and minimize morbidity associated with sickle-cell disease, while significantly improving the quality of life of sickle-cell disease patients and their families in the African Region.

The specific objectives are to:

- reinforce the training of health care personnel at every level of the health pyramid in Africa
- prevent and effectively treat acute and chronic complications
- reduce SCD-related premature mortality especially in children under 5 years of age
- ensure effective education of people living with sickle-cell disease and their families
- work together to standardize the practice and day-to-day work of practitioners, from the first level to centres of excellence.

2. Understanding sickle-cell disease

2.1 Definition of sickle-cell disease

Sickle-cell disease is an autosomal recessive inherited disorder characterized by the presence of an abnormal haemoglobin called haemoglobin S in red blood cells. The latter is responsible for the sickling of red blood cells in deoxygenated state.
Severe forms of SCD include haemoglobin SS (sickle-cell anaemia) due to homozygous inheritance of HbS and HbS/β^0 thalassemia due to co-inheritance of HbS with the β^0 thalassemia mutation. Other forms include co-inheritance of HbS with other β-globin gene mutations such as haemoglobin C, haemoglobin D-Los-Angeles/Punjab or β^+ thalassemia.
A distinction is made between heterozygous condition or sickle-cell trait, which is generally asymptomatic.
The sickle-cell trait is NOT a disease.

2.2 Epidemiology (global and Africa)

SCD is most prevalent among people of African descent. The global prevalence of SCD across all ages increased from 5.46 million to 7.74 million cases from 2000 to 2021. A “sickle belt” has been described in Africa, stretching from the southern Sahara to the northern Zambezi, along an area between the 15th parallel north, and the 20th parallel south; this area is also malaria-endemic (Annex 1). Hb SC composite double heterozygosities are mainly found in Black Africa in the Volta basin (Mali, Niger, Burkina Faso), due to the frequency of haemoglobin C in these populations. As for HbS/β thalassemia, it is mainly observed in the Mediterranean basin, where β- thalassemia is particularly common.

The prevalence of the sickle-cell gene in Africa varies from 10% to 40%. Sickle-cell disease is present in all countries where black populations have emigrated, including the United States of America, the West Indies, France, Belgium and England. It is also found in the Mediterranean basin (Maghreb, southern Europe), the Middle East (Saudi Arabia) and especially in India.

In retrospective, between 2000 and 2021, newly diagnosed SCD cases increased worldwide at the rate of 382 per 100 000 live births, from 453 000 to 515 000. The rate increase varies according to genotype, with 76.5% of births being SS and Sβ°, 19.6% SC and 3.9% Sβ+.

Increased SCD mortality is reported worldwide, but the highest mortality rate is found in sub-Saharan Africa, where 29 400 patients with sickle-cell disease died in 2021, representing an increase of 30.1% since 2000.
SCD accounts for 2.2% of all under-five deaths. In sub-Saharan Africa (SSA), SCD is ranked 11th among all-cause mortality.

2.3 Pathophysiology

A genetic alteration of haemoglobin characterizes sickle-cell disease due to mutation of the β globin gene, leading to the substitution of glutamic acid by valine in position 6 of the β globin chain (β6Glu→ Val).

The mutation leads to abnormal haemoglobin (haemoglobin S) molecules, which leads to polymerization (precipitation of haemoglobin) in the deoxygenated state. Precipitation of Hb can stiffen and deform the red blood cell, giving it its characteristic banana shape (sickle-shaped). Inflammation triggered by sickling promotes the adhesion of neutrophils and activates platelets. Sickle red blood cells also attach to the endothelial surface and to each other, which promotes vaso-occlusion in different organs and tissues. This leads to ischaemia and pain. Blood viscosity and stasis, consequence of red blood cells' aggregability and higher concentration, leads to hypoxia and acidosis, resulting in a vicious circle.

The lifespan of the sickle cell is shortened from 120 days to about 30 days, leading to haemolysis, which causes anaemia and jaundice (haemolytic anaemia). The vaso-occlusion in the spleen leads to splenic dysfunction, which predisposes the patient to infection. All organs can be affected by vascular occlusion, making sickle-cell disease a multisystem disorder.

Diagram of genetic inheritance

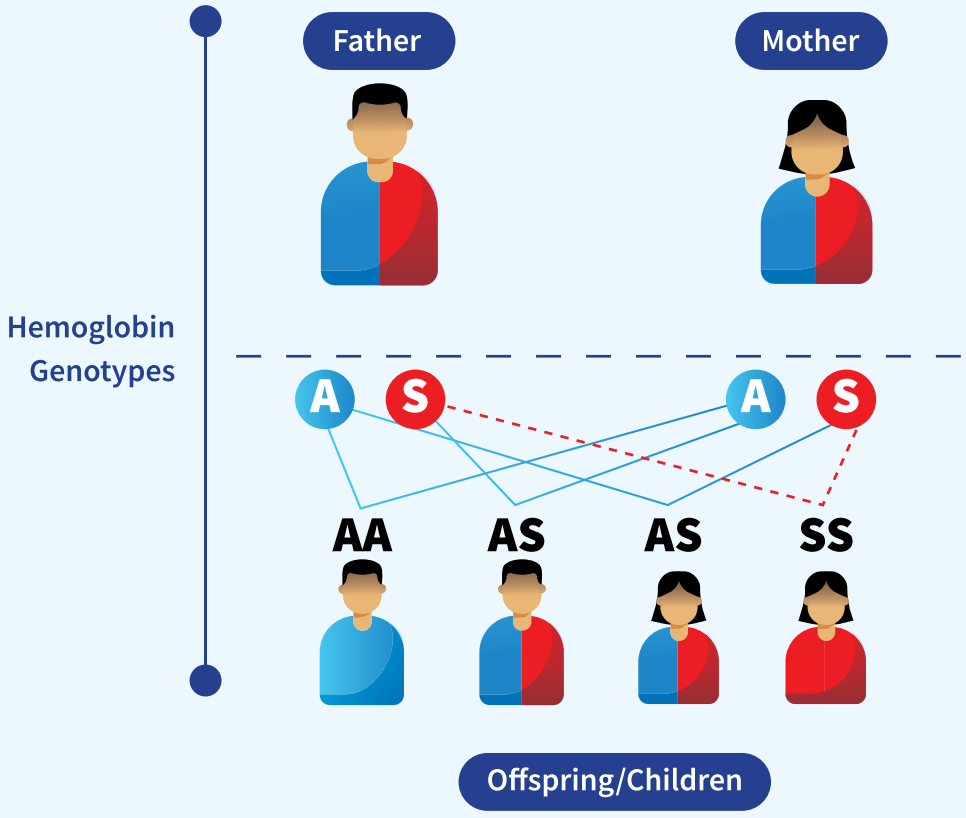

Fig. 1. Inheritance pattern of sickle-cell anaemia

Factors modifying the sickling process

Several factors that influence the pathophysiology of SCD increase the risk of red cell sickling, for example, dehydration, hypoxia or acidosis. Undernutrition, which impairs the body's defence capacity, particularly in children, is a risk factor. In addition, all forms of physical or psychological stress are all factors associated with morbidity. Exposure to malaria is a risk factor for morbidity and mortality.

Association with other haemoglobin abnormalities modifies the clinical manifestations of sickle-cell disease. Fetal haemoglobin has a protective role against SCD, and this is well illustrated in sickle-cell children, who are born with fetal haemoglobin levels well above those of haemoglobin S, and only manifest the disease when haemoglobin S levels exceed those of fetal haemoglobin.

The absence or neglect of regular health monitoring due to geographical, financial, or technical difficulties in accessing care can lead to the onset of often fatal multi-organ failure.Clinical features

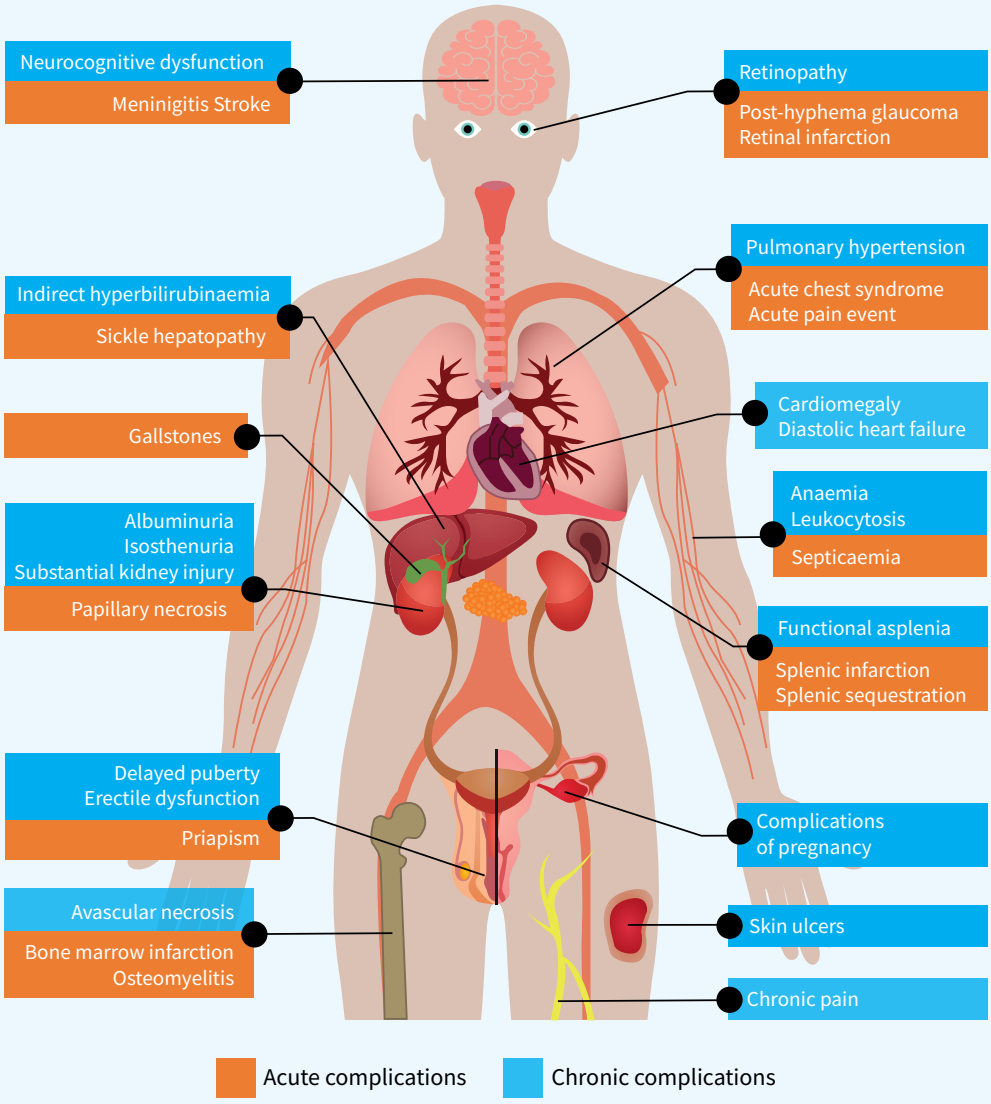

Fig. 2. Diagram of body showing SCD clinical features

The WHO Regional Office for Africa

The World Health Organization (WHO) is a specialized agency of the United Nations created in 1948 with the primary responsibility for international health matters and public health. The WHO Regional Office for Africa is one of the six regional offices throughout the world, each with its own programme geared to the particular health conditions of the Member States it serves.

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