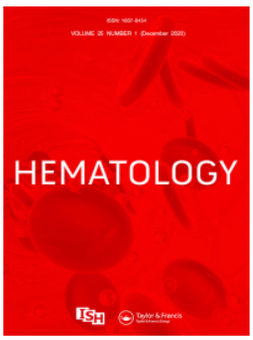

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Overview of current progress and challenges in diagnosis, and management of pediatric sickle cell disease in Democratic Republic of the Congo

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ABSTRACT

Objectives: Sickle cell disease (SCD) encompasses health complications, primarily affecting the hematologic system and leading to high death rates in childhood. As a rule, the World Health Organisation (WHO) stepwise gold-standard about the strategies for prevention, diagnosis, and treatment of SCD must be multidimensional. This overview aimed to highlight current advances and challenges linked to strategic issues, diagnosis, the prevalence, and treatment of pediatric cases in Sub-Saharan Africa, particularly the Democratic Republic of the Congo.

Methods: We searched data on Google Scholar, Medline, PubMed, Science Direct, Scopus, and ResearchGate.

Results: The laboratory diagnosis of SCD has progressed from conventional electrophoresis to rapid point-of-care tests that allows early neonate screening. HemoTypeSC™ is an affordable test for neonatal screening in DRC. The pediatric SCD prevalence in Sub-Saharan Africa lay within 1–7.7% of homozygous(SS) and 15–40% of the heterozygous(AS) forms of SCD, depending on the method used and the ethnic population tested. Various supportive management protocols for comorbidities and complications exist, but they are not standardized in the Region.

Conclusion: Notwithstanding some progress accomplished, the disease is still challenging in Sub-Saharan Africa due to limited early diagnostic testing and a lack of specific medications. There is a need for harmonizing therapeutic protocols and conducting controlled valid clinical trials.

KEYWORDS

Sickle cell disease; pediatrics; diagnosis; prevalence; management; Sub-Saharan Africa; DR-Congo

1. Introduction

Hemoglobinopathy is defined as a blood pathology caused by genetic mutations that lead to qualitative and quantitative changes in structure and quantity of hemoglobin (Hb) chains [1]. To date, over a thousand variants of hemoglobin are described in the HbVar database. Not all these variants are clinically significant [2]. Globally, hemoglobinopathies fall into two main groups, including structural variants of hemoglobin (abnormal hemoglobins) and thalassemia syndromes (α-and β-thalassemia). Hemoglobin is a tetramer made up of two chains of α-globin and two chains of β-globin working together with heme to transport oxygen in the blood [1]. Normal adult hemoglobin (HbA) is referred to as αA2βA2 [1]. Variant hemoglobin is derived from genetic mutations in the structural genes of α-globin (HBA1 or HBA2) or β-globin (HBB) (exons).

Quantitative changes such as insertions of amino acids, deletions or mutations in intermediate sequences (introns) correspond to thalassemia and lead to a decrease in globin chain production. There are hundred beta-thalassemia mutations around the world. In deletion-type thalassemias, the number of deletions of the α-globin gene correlates with the severity of the disease. A deletion of the α-globin gene is common place (also called a silent carrier), while a deletion of two α-globin genes (α-thalassemia trait) and three deletion of the α-globin gene (HbH disease) have various clinical and haematological characteristics. A deletion of four genes from α-globin (Hb Bart's Hydrops fetalis) is serious and is usually not compatible with life.

The qualitative changes correspond to amino acid substitutions leading to structural abnormalities of β-globin. The most frequently observed structural amino acid substitutions for β-globin include HbS (c.20A > T, p.E6 V), HbC(c.19G > A, p.E6 K), HbD(c.79G > A, p.E26 K), HbE(c.364G > C, p.E121Q), and HbO

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(c.364G > A, p.E121 K) [1, 3]. HbS is a recessive genetic disease; both copies of the gene must contain the mutation for a person to have HbSS sickle cell disease (SCD), also called sickle cell anemia (SCA). If an individual has only one copy of the mutated gene, he is said to be a carrier of the sickle cell trait (SCT).

The incidence of SCD is estimated between 300,000 and 400,000 newborns worldwide each year, most of them in sub-Saharan Africa [4]. It was assumed that in areas endemic for malaria, HbS carriers were naturally selected because the trait confers some resistance to malaria. Their Red Blood Cells (RBC), containing abnormal hemoglobin, tend to sickle when infected with the malaria parasite. Following natural selection linked to a positive selective effect of heterozygotes by malaria, several mutations in globin genes have persisted and have seen their frequency increase [4]. These include the βS mutation in sub-Saharan Africa, βC in West Africa, βD-Punjab in India and α-thalassemia in the Mediterranean region [4]. The highest frequency of the βS allele occurs in low-lying tropical areas. In contrast, the βC allele is found almost exclusively in people of West African descent (Burkina Faso and northern Ghana) [4]. However, this does not mean that natural selection is the only factor necessarily increasing these frequencies, as there are certainly other factors such as population growth in regions of the world with epidemiologically high frequencies of β-globin mutations.

A variety of strategies have been developed to reduce the incidence and prevalence of SCD, including prenatal counseling and education. As life-threatening events can occur in children with SCD from three months of age, early diagnosis of newborns is necessary to establish preventive measures. Although the regions of sub-Saharan Africa are the most affected, newborn screening programs are not implemented satisfactorily [5–7]. The disease is associated with high death rates before the age of five [8]. Concomitant nutritional deficiencies, infections, or exposure to environmental toxins exacerbate chronic anemia in children with sickle cell disease. The resulting relative anemia is associated with an increased risk of stroke, reduced cognitive function and impaired growth [9]. During the sixtieth session of the Regional Committee for Africa [10], held in Malabo, Equatorial Guinea, from August 30 to September 3, 2010, the participants defined six objectives for 2020 which are: (a) implementation of a simple national SCD control program in at least 50% of the 23 Member States; (b) adoption of the concept of comprehensive management of SCD health care by 25% of countries; (c) the establishment of an SCD surveillance system with adequately trained personnel by at least 50% of all nations.

The Democratic Republic of the Congo (DRC) is one of the three African countries most affected by SCD, counting 30,000–40,000 newborns with the HbS trait each year [5,11]. Prevalence and mortality data on SCD in children are challenging due to low diagnostic testing and a lack of specific medications. This article aimed to highlight successes/challenges related to the strategic targets, diagnosis, prevalence, and treatment of pediatric cases in DRC compared to other countries in sub-Saharan Africa.

2. Literature search method

The study was an Internet-based search on Google Scholar, Medline, PubMed, Science Direct, Scopus, and ResearchGate database, including original and reviewed articles in English or French. Using keywords: 'Sickle cell anemia' OR 'sickle cell disease' OR 'sickle cell trait' OR 'sickle anemia' AND 'Africa Pediatric SCD' OR 'neonatal screening' AND 'Sub Sahara Africa 'OR 'DR-Congo.' We extracted publications on DRC and neighboring countries for analysis and used gold-standard recommendations from other papers for discussion. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram is presented in Figure 1.

3. Findings

3.1. Achievement of global management strategic goals

Recently, the Seventieth session of the WHO Regional Committee for Africa was held virtually on 25 August 2020 and resumed on 24 November 2020 [12]. It was held under the special procedures to regulate the conduct of the virtual session of the Regional Committee for Africa. Special events on the COVID-19 response in the region took place on both dates. Table 1 summarizes some key points.

3.2. Advances and challenges on laboratory diagnostic in DRC

A wide variety of methods are available worldwide to diagnose homozygous SS, heterozygous AS, SC disease, and HbS-thalassemias-α. Alongside the HbS smear and solubility tests, there are currently five groups of tests commonly used to distinguish variants of hemoglobin mutations. We have hemoglobin electrophoresis(CAE), isoelectric focusing (IEF), capillary isoelectric focusing(CIEF), capillary zone electrophoresis(CZE), liquid chromatography (HPLC), mass spectrometry(MS), Immunological tests(ELISA), and DNA sequencing. HbS is largely predominant in RDC. The prevalence of HbC, HbE and other Beta-globin variants is expected to be very small. Therefore, the requirement of techniques allowing the identification of other variants than

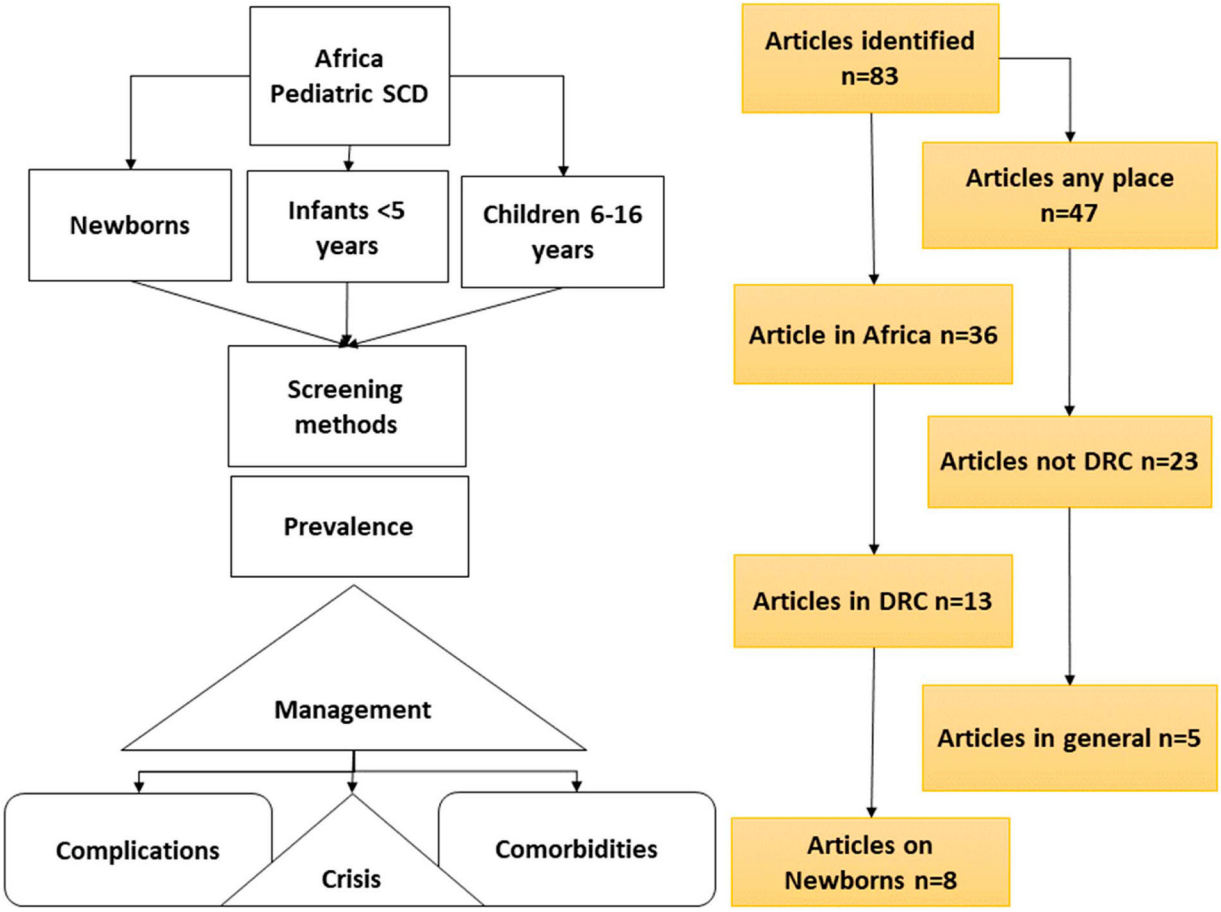

Figure 1. PRISMA flux for keywords and articles retrieval.

HbS is initially of poor interest. Table 2 shows the most methods used in the region for screening only AS, AC, SS, SC, CC, withdrawing other variants. The most conventional methods used in resource-limited countries including DRC to identify AS and SS are the microscopic peripheral smear of HbSS and the sickle cell solubility test [13]. Although simple, these tests do not differentiate between different hemoglobinopathies SC or HbS-αThal. Currently, many countries have better testing that allows for better identification including non-sickling genotypes (AS, AC, SS, SC, CC, A2, E, C, D).

Table 1. Progress and challenges since last regional committee recommendations.

Strategy target	Progress and challenge
Functionality of national SCD control programmes in high-burden Member States	All 23 high-burden Member States established a designated unit for SCD in their respective ministries of health including DRC.
SCD Included in the current national health plans	Done in eighteen countries. Not in Burundi, Comoros, Mauritania, Senegal and Sierra Leone.
Annual State Budget allocated	All have implemented clearly defined national SCD control programmes for prevention and control of SCD. Actual funding from the annual State budget is allocated for SCD in only eight Member States, DRC not included. For newborn screening or mass screening for SCD, the budget was allocated only in Burkina Faso, Kenya, Liberia, Niger and Nigeria. For surveillance, monitoring and evaluation of SCD activities, only Burkina Faso, Liberia, and Nigeria did it. Capacity building for prevention and management of SCD, only Seven Member States allocated the budget, DRC not included. For research related to SCD, only Benin, Burkina Faso, Liberia, Mali, Togo and Zambia successed.
Newborn screening for SCD	it is being practised in 12 Member States at subnational level. In Mali, DRC, Uganda and Ghana the samples for newborn screening are collected at all levels of the health system and transported to the tertiary facilities. In other countries, the services are generally provided only in tertiary health facilities. In Burkina Faso and Uganda, SCD newborn screening is integrated into HIV screening programmes. In six other Member States, newborn screening for SCD is integrated into Reproductive, Maternal, Newborn and Child Health(RMNCH) programmes. These linkages improve early detection and management of SCD.
Prevention and treatment	Folic acid prophylaxis for SCD patients is available in many Member States that responded, except in Angola, Burundi, Central African Republic and Gambia Hydroxyurea was reported in 11 Member States, DRC included.
Strategic information, surveillance and research	Only 10 Member States had data on SCT prevalence in newborns and adults.

Table 2. Laboratory methods for AS, AC, SS, SC, CC screening.

Method principle	Best identification AS, AC, SS, SC, CC	Newborn HbF	Cost	POC	Quantitative	Available in DRC
Conventional techniques						
Microscopy: sickling	AS, SS	No	Low < 1$	No	No	Yes
Solubility: precipitation	AS, SS	No	Low	No	No	Yes
Hemoglobin electrophoresis						
CAE	AS, SS	No	Mild	No	No	Yes
CZE	AS, SS	Yes	Mild	No	Yes	No
IEF	AS, SS, SC	Yes	Mild	No	No	Yes
CIEF	AS, SS, SC	No	Mild	No	No	No
HemeChip	AS, SS, SC	Yes	Mild	Yes	Yes	No
Density-based separations						
AMPS	SS	Yes	Mild	Yes	No	No
ELISA Immunology assays						
Sickle SCAN™	AS, SS, SC	No	Mild	Yes	No	Yes
HemoTypeSC™	AS, AC, SS, SC, CC	Yes	Mild	Yes	No	Yes
Paper chromatography						
PBC	AS, SS	No	Mild	No	No	No
HPLC and MS						
HPLC CE	AS, SS, SC	Yes	High	No	Yes	No
LC CE	AS, SS, SC	Yes	High	No	No	No
HPLC-ESI-MS	AS, SS, SC	Yes	High	No	Yes	No
Molecular methods						
Targeted approach	Many variants	Yes	High	No	No	No
Globin gene sequencing	Many variants	Yes	High	No	No	No

Newborns with β^S mutation take several months after birth to produce significant detectable amounts of HbS. Also, fetal hemoglobin (HbF) prevents polymerization and hemolysis at a high enough concentration within each RBC [14]. Thus, some techniques do not fit for newborns due to the predominance of HbF at birth; if used at birth, they may produce false-negative results if the HbS is less than 10% of total hemoglobin [13]. Specific tests for neonates that are feasible in DRC may include Isoelectric Focusing (IEF) and HemoTypeSC™ [15,16].

IEF has a high resolution that can distinguish a more significant number of Hb variants [17–19]. However, due to the high number of bands resulting from this higher resolution, the IEF results are more challenging to interpret and more expensive. Despite these challenges, the IEF may be the standard method for newborn screening. The diagnosis is possible with a minimal sample volume or even an eluate from a dried bloodstain [17,18].

HemoTypeSC™ uses monoclonal antibodies to distinguish between HbAA, HbAS, HbAC, HbSS, HbSC, and HbCC. The presence of high concentrations of HbF does not interfere with HemoTypeSC™ result at in neonates. A prospective study by Kasai et al.[15] in Kisangani(DRC) confirmed that HemoTypeSC™ remains the only rapid test indicated for neonatal screening.

Following the manufacturer's instructions (Figure 2), a sample of 1.5 µL of blood was collected by a puncture in the heel from the neonates or in the finger from adults using a thin needle (lancet) regularly used locally for the blood sample. The test result takes 20 min. It costs <2USD per test, does not require electricity to function, requires no instrumentation, thus making it ideal for most low-resource settings [15,20]. Its accuracy for detecting all relevant hemoglobin phenotypes/genotypes have been validated in pilot studies from the U.S.A., Europe, and Africa [20].

HPLC and MS have been used abroad to validate the results obtained locally [21]. These machines are relatively expensive and are not readily available in DRC. *DNA amplification and sequencing* can detect variant β-globin mutations that produce abnormal Hb [22,23]. However, it is generally more expensive than the methods described previously.

3.3. Prevalence of SCD in DRC and neighboring countries

Table 3 shows some data reported in the literature on DRC and neighboring countries. The pooled mean SCD prevalence ranges within 0.12–7.7%, and the carriers SCT within 5.62%–24.6% [15,19–37]. In DRC, the prevalence range is 0.96–4.5% for SCD and 5.6–24.2% for SCT [24–27]. Some differences observed depend on the size sample and the method used. For example, in Kisangani, Batina et al. [19] reported 0.96% of newborns with SCD ($n = 520$ umbilical cord blood), using IEF test in 2011. Kasai et al. [15], in the same city, reported 1.01% of newborns with SCD ($n = 70$ samples of heel-picked samples), using the HemoTypeSC™ test. In all the neighboring countries to DRC, the cases of HbC phenotype are seen in Rwanda [25] and Angola [31]; these appear mainly in western countries, Nigeria [35], Ghana [34], Burkina Fasso [33], and Mali [36].

3.4. Clinical management approaches of pediatric SCD

The WHO recommended that SCD should be managed at different levels of care through the use of simple, cost-effective, and affordable strategies and

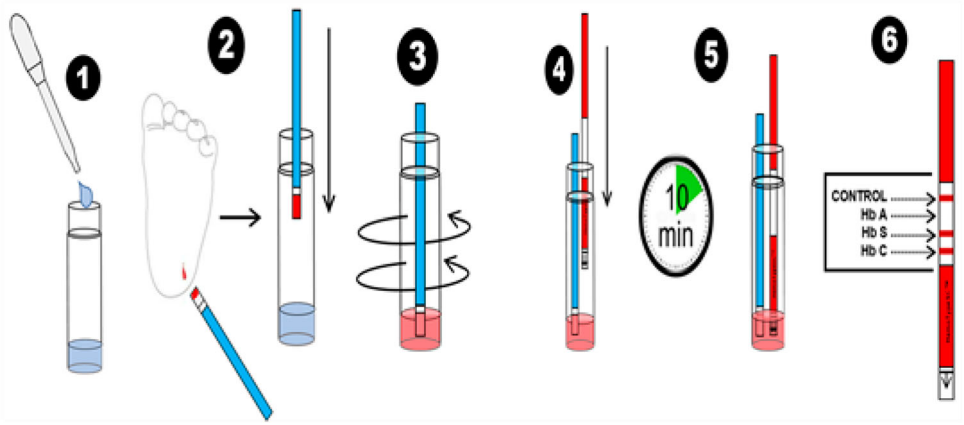

Figure 2. Manufacturer's instructions for HemotypeSC™ (Kasai et al. 2019).

Table 3. Phenotypic profile according to the various studies.

Country	Ref	Population	Sample	% HbSS	% HbAS	% HbAC	Method
Angola	[31]	1 year–5 years	36453	1.5	21.0	0.019	CZE, IEF
Burkina Faso	[33]	Median 9 years	9201	0.09	0	0.13	–
Congo (Brazza)	[26]	Newborns	1119	0.9	16.8	0	IEF, HE, HPLC
DRC (Kinshasha)	[23]	4–159 months	807	4.5	5.6	0	SickleSCAN
DRC (Kisangani)	[19]	Newborns	520	0.96	23.3	0	IEF
DRC (Kisangani)	[15]	Newborns	70	1.01	24.2	0	HemoTypeSC™
DRC (whole)	[24]	Newborns	31204	1.4	16.9	0	IEF
Gabon (Libreville)	[27]	>15 years	4250	–	21.1	0	IEF; HPLC
Gambia	[32]	10 Mo–6 years	536	0	15.9	0	DNA
Ghana (Northern)	[34]	6 Mo-9 years	2108	0.3	7.4	19.7	PCR
Kenya (Bondo)	[30]	0–36 months	2774	0.6	22	0	HE
Mali (Bamako)	[36]	Newborns	2489	0.24	5.6	0.26	IEF, HPLC
Nigeria (Garki)	[35]	Newborns	534	2.1	24	0.70	–
Rwanda	[25]	Newborns	1825	0.18	2.54	0.09	ELISA
Sudan	[29]	>5 years	400	3.5	11.3	0	HE
Tanzania (Muhimbili)	[37]	Newborns	3981	0.8	12.6	0.7	IEF
Uganda	[28]	<5 years	1000	9.8	18.2	0	HemoTypeSC™

technologies that are accessible to all patients including those in the rural communities, where the bulk of Africans reside [20]. As a rule, the WHO stepwise gold-standard about the strategies for prevention, diagnosis, and treatment of SCD must be multidimensional [38].Table 4 summarizes the data reported by different researchers in DRC on SCD diagnosis, clinical symptoms, Transfusions, Medicines, Curative therapies, Cultural beliefs, and Infrastructure limitations.

3.4.1. Clinical symptoms and management of complications in pediatrics

SCD has several manifestations, which include frequent painful episodes, bone infection and infarction, stroke, renal and cardiopulmonary disorders and other chronic organ. Also, they are more prone to severe anemia and infections. These manifestations often lead to increased morbidity and early mortality, especially among patients in resource-poor parts of world [8,20]. It is essentially the hand-foot syndrome and acute anemia that are found in about half of the cases. Pain is the hallmark of SCD infants, but their high HbF levels spare them from early attack. The first episode of pain often occurs in the small bones of the hands and feet (dactylitis) by 2 years [5]. A study conducted in Kinshasa [5] showed that in 52.7% of cases, the hand-foot syndrome was the first most common presentation revealing the disease, and the age at the first painful attack was 18.2 ± 15.2 months. The most complications associated with SCD were hepatomegaly (53.9%), splenomegaly (41.7%), Splenic sequestration (7.4%), and adenotonsillar hypertrophy (34.8%) [39]. Acute Chest Syndrom (ACS) is a life-threatening complication with a maximum incidence in infancy. Etiologies of ACS include a pulmonary fat embolism, infection, sickle phenomenon, fluid overload, and atelectasis that occur due to hypoventilation to overdose or inadequate pain control. Pulmonary hypertension is associated with increased mortality in adult SCD patients, but this association has not been demonstrated in pediatric SCD patients [48]. Cross-sectional clinic-based data report 2.9% to 16.9% stroke prevalence among children with SCD in Africa [44]. While defects in urinary concentration (hyposthenuria) and glomerular hyperfiltration are common in young SCD patients, SCD nephropathy is relatively rare in pediatric SCD patients, increasing incidence during adolescence [45]. Although uncommon in sub-Saharan Africa, one study reported 31% cases of nephropathy in Tanzania at the Est neighbor of DRC.

Table 4. Data reported by different researchers.

Intervention	Indicators	*N*	Observation	References
Diagnosis	Neonate routine practice	807	0%	[5, 24]
	After pain attack		54.8%	[24]
	Before 2 years	247	71%	[39]
Symptoms	Diagnosed by dactylitis, pain attacks	166	52.7%	[5]
	Peak incidence age in months	807	7–36	[24]
	First presentation age months		42.7 ± 29.7	[24]
	First pain crisis age months		18.2 ± 15.2	[5]
SCD complications	Children mean age (8.4 ± 4.9)			
	Hepatomegaly	256	53.9%	[39]
	Splenomegaly		41.7%	[7]
	Vasoocclusive crisis (VOC)		66.4%	[5]
	Adenotonsillar hypertrophy	807	34.8%	[24]
	Severe hemolysis		53.1%	[24]
	Hand foot syndrome		52.7%	[24]
Blood transfusions	All ages	450		
	Cases frequency		74.0%	[39]
	Age of first transfusion months		29.2 ± 27.6	[22]
	Number of transfusion per year		4 ± 3	[5]
Infection prophylaxis	Infants Vaccinations & Penicillin			
	Both vaccination & Penicillin	198	1.5%	[40]
	Hemophilus influenza vaccinated		0%	[6]
	Streptococcus pneumoniae vaccinated		61%	[39]
	Salmonella sp vaccinated		0%	[7]
	Hepatatis B virus (HBV) vaccinated		16%	[39]
	Antibiotic prophylaxis cases		35%	[7]
Pain management	Infants			
	Age at the first pain attack in months		18.2 ± 15.2	[5]
	Emergency care	234	50%–60%	[39]
	Painkillers NSAIDs		100%	[5]
	Hydroxyurea taken irregularly	234	45%	[39]
Cultural beliefs and education	Parents with good awareness		38%	[41]
	Students know pre-marital screening		7.7%	[42]
	Students ignore any preventive measures		25.4%	[42]
	Physicians trained on SCD		1%	[43]
	Physicians knowing management of VOC		46%	[43]

Some factors like urinary schistosomiasis and acute malnutrition increase the risk for renal dysfunction in children with SCD in SSA [46]

In DRC, managing all complications is a big challenge due to a lack of infrastructure and sufficient qualified caregivers. Pain killers often prescribed are Nonsteroidal Anti-inflammatory Drugs (NSAIDs). When treating pain in a hospital, an integrated approach is used that includes intravenous fluids to treat dehydration, and intravenous pain relievers NSAIDs. No study mentioned using narcotics in DRC. Also, techniques of non-pharmacologic pain management, including warming compress, relaxation, and breathing exercises are used. At the hospital level, oxygen therapy has no documented analgesic effect [47]. It is proposed in the event of desaturation to maintain arterial oxygen saturation greater than or equal to 95%. As requirements, oxygen therapy should not mask the progressive onset of hypoxemia of acute chest syndrome. Hydroxyurea is the only drug approved by the Food and Drug Administration (FDA) to treat adults with SCD [48–50]. In pediatric SCD patients, the initial dose of hydroxyurea is 15–20 mg/kg/day and is increased in 5 mg/kg/day increments until the target dose of 30–35 mg/kg/day is reached [48,50]. Some studies show that in DRC, 45.0% of patients with more than three severe painful attacks per year were eligible for hydroxyurea, but the drug was taken irregularly [39]. The first challenge is that 82% of drugs are purchased by parents [39], the second major challenge is the exorbitant price of this product around 15usd [49]. In Congo Brazzaville, of 1024 children monitored for SCD, 107 (10.4%) had received hydroxyurea in recurrent anemic attacks [48]. Therapeutic compliance was good in 89.5% of them; a rapid and lasting clinical improvement was noted in the majority of patients.

3.4.2. SCD diagnosis

Studies show that newborn screening in the DRC is still not in everyday practice [4–6]. One cross-sectional study [24] carried out in four hospitals in Kinshasa on 807 patients suffering from anemia (Hb < 6 g/dL) shows that 54.8% of patients were SCD diagnosed after experiencing pain attacks. One study [39] conducted among 247 children attending the Pediatric Yolo Centre in Kinshasa reports that among 71% of patients diagnosed before the age of 2 years, none was at the neonatal period. Early neonatal screening is still embryonic and limited to research projects in university hospitals.

3.4.3. Blood transfusions

A first stroke can be prevented by transfusions in SCA children with abnormal results on transcranial Doppler ultrasonography [44]. According to the American Society of Hematology's guideline, blood transfusion could help to prevent secondary stroke by increasing

the hemoglobin above 9 g/dL at all times and maintaining the HbS level at 30% of total hemoglobin [51]. Two studies conducted in low-resource settings, children with SCA and strokes who did not receive regular blood transfusion had an overt stroke recurrence rate of 29 per 100 person years, with ≥50% of children having acute stroke recurrence in 2 years [51]. In Kinshasa, a study with 168 subjects showed that 74.0% of SCD children had previously received blood transfusions. The age at the first transfusion was 29.2 ± 27.6 months [24]. Acute anemia in SCD children is most often due to Acute splenic sequestration (ASS), acute transient erythroblastopenia related to erythrovirus infection (parvovirus B19), and hyperhemolysis. If recurrent ASS occurs before 2 years, patients can be maintained with chronic monthly blood transfusions to keep HbS below 30% until reaching a safer age for splenectomy.

3.4.4. Preventive and curative antibiotherapy

Concerning vaccination and prophylactic antibiotherapy, the study by Kondani et al.[6] showed nobody had received Hemophilus influenzae or salmonella sp vaccines, but 61% had received *Streptococcus pneumoniae vaccine*. One study showed that of 168 pediatric patients surveyed in Kinshasa, only 35.0% had been regularly taking penicillin antibiotic prophylaxis [39]. Advisory Committee on Immunization Practices (ACIP) recommends to give, at 2 and 5 years old, the 23-valent pneumococcal vaccine (Pneumovax®) and the quadrivalent meningococcal vaccine to pediatric patients at increased risk of invasive meningococcal disease [52]. Penicillin prophylaxis should be started before 2 months at an oral dose of 125 mg twice daily and increased to 250 mg twice a day at 3 years to take into account the child's physical growth [53].

3.4.5. Curative treatment

Currently, the only cure available for SCD is Hematopoietic Stem Cell Transplant (HSCT). In pediatric patients, the 3-year survival after HSCT is 90% compared to 62% in adult SCD patients. SCD matched donor transplants have excellent overall survival (93–97%) and good event-free survival (85%); however, less than 20% of SCD patients have a suitable sibling donor. Gene therapy has made impressive recent progress and has the potential for treating a wide range of diseases, many of which are essential to Africa [51]. However, due to a lack of direct public funding and skilled personnel, direct research on gene therapy in Africa is currently limited, and resources to support the endeavor are modest [54]. Out of the 54 African countries, HSCT is available only in Algeria, Egypt, Morocco, Nigeria, South Africa, and Tunisia.

3.4.6. Cultural beliefs and education

For education and counseling, a cross-sectional study [43] involving 158 SCD patients consulted in 2017 at general hospitals in Kisangani shows that 44.9% of respondents believe that SCD has a demoniac origin; 77.8% think the church and traditional healers are more suitable than formal health systems. Among students of the University of Kisangani [42], only 7.7% cited pre-marital screening as a preventive method, and 25.4% could not mention any prevention measure, meaning that students' knowledge regarding SCD is inadequate and needs improvement through education programs and motivational campaigns. Parents must learn to recognize the first signs of a severe complication to get their child to the emergency hospital and first care to apply [37]. For example, recommend great alkaline drinks than usual in documented tubular acidosis at the onset of a painful attack; a hot water bottle on the painful area can help reduce pain.

4. Conclusion

This review has shown significant progress accomplished, yet many challenges persist. Neonatal screening is feasible only in a few countries and mainly in the capitals where resources allow it. The performance of POC tests like HemotypeSC™ makes it possible for systematic neonatal screening. However, there is no guaranteed free-testing program for sure in low-income countries. Counseling and prenuptial testing is an absolute necessity without which the trait will continue to cause high mortality. There are some specialized centers devoted to managing pediatric SCD patients. Still, the scarcity of financial resources and the poverty of parents make it difficult to assure adequate care of SS screened children.

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