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# Major Sickle Cell Disease in Pediatrics from 2023 to 2024: Study of Morbidity and Prognostic Factors at Bouaké University Hospital

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## Abstract

**Introduction:** Since 2017, a specialized care unit for children with sickle cell disease has been established at the Bouaké University Hospital (CHU). In this unit, children with major sickle cell disease are followed up. The objective of the study was to assess the morbidity associated with this condition to improve clinical practices and outcomes. **Methods:** This was a retrospective cross-sectional analytical study conducted from April 2023 to April 2024 in the pediatric sickle cell care unit of Bouaké University Hospital. All children with major sickle cell disease who had been followed for more than 12 months and had been hospitalized at least once in the unit were included. The variables studied were sociodemographic, diagnostic, therapeutic, and related to disease progression. Variable comparisons were performed at a significance level of $p \leq 5\%$. **Results:** Of the 272 children followed for sickle cell disease, 81 had a major form (30%), among whom 45 were included in the study (16.5%). There were 25 boys and 20 girls. Seventy-one percent were over 5 years old. Their phenotypes were SFA2 (48.9%), SC (28.9%), or SS (22.2%). Hydroxyurea therapy was administered in 24.4% of cases. Treatment adherence was observed in 64.4%. Seventy-three point three percent had been hospitalized at least twice. The causes of hospitalisation were infection (84.4%), severe anemia (57.8%), and acute chest syndrome (2.2%). Hydroxyurea use was significantly associated with a lower number of hospitalisations ($p = 0.0034$). **Conclusion:** Treatment with hydroxyurea and good therapeutic adherence may help re-

duce the number of hospitalisations and complications.

**Keywords**

Sickle Cell Disease, Child, Prevalence, Treatment, Cote d'Ivoire

## 1. Introduction

Despite significant progress made in high-income countries, sickle cell disease remains a major public health concern in many resource-limited countries. Ranked as the fourth global public health priority by the United Nations after cancer, AIDS, and malaria [1] this genetic disorder affects between 3% and 3.6% of the global population, with more than 300,000 children born each year, over 75% of whom are in sub-Saharan Africa [2]. While pediatric mortality associated with major sickle cell syndromes (MSS) dropped from 1.1 to 0.13 per 100 patient-years between 1980 and 2010 in industrialized countries [3], it remains a major concern in underserved regions. A meta-analysis of more than 15 publications estimated the overall mortality rate at 0.64 per 100 patient-years, with a particularly alarming rate of 7.3% in Africa [4]. The WHO highlights that up to 16% of homozygous children may die before the age of five in some West African countries [5]. In Côte d'Ivoire, sickle cell disease is also highly prevalent, with the S hemoglobin gene found in 11.71% of children [6]. At the Bouaké University Hospital (CHU de Bouaké), a dedicated care unit was opened in 2017. Between 2017 and 2023, 272 children with sickle cell disease were followed there, including 81 with major forms. A preliminary study conducted in 2022 reported a hospital prevalence of 0.45% for the major form [7].

In response to this situation, several strategies were implemented in 2023. These included training doctors in the management of children with sickle cell disease, developing a therapeutic protocol, strengthening staff capacity, and distributing free hydroxyurea and pain medications to the most vulnerable families. Did these targeted interventions lead to a tangible improvement in the clinical and evolutionary profile of hospitalized children with sickle cell disease at Bouaké University Hospital? To answer this question, we conducted this study, which aimed to assess the profile of hospitalized children with sickle cell disease and identify potential associated factors to improve their quality of life.

## 2. Methods

This was a retrospective, descriptive, and analytical study in the Pediatric Department of Bouaké University Hospital, from April 1, 2023, to April 30, 2024. It took place in the sickle cell care unit for children and adolescents, "PLO KOUIE JEANNOT," within the pediatric department at the University Hospital of Bouaké. This unit was established in 2017, with approximately 400 registered children and an active cohort of 200 children and adolescents. It is overseen by a university-affili-

ated physician, assisted by three other physicians who hold a university diploma in Major Sickle Cell Syndromes.

The unit's activities include community awareness and screening campaigns (twice a year), therapeutic education sessions (once per quarter), preventive care (quarterly or monthly consultations depending on the symptomatology, along with an annual check-up for complications), and curative care in case of complications (consultation or hospitalisation).

The study included all children (aged 6 months to 15 years) diagnosed with major forms of sickle cell disease, defined as hemoglobin phenotypes SS, SC, or S$\beta^{\circ}$-thalassemia confirmed by hemoglobin electrophoresis, followed in the unit during the study period. Sampling was exhaustive. All children with major sickle cell disease who had been followed in the department for at least 12 months and had a history of hospitalisation during the study period were eligible. Exclusion criteria were lack of parental consent, incomplete medical records, loss to follow-up for more than 6 months, or missing key laboratory or hospitalisation data. Among the 81 children meeting the eligibility criteria, 45 were included: 21 were excluded due to incomplete medical records, 10 were lost to follow-up, and 5 had missing essential data. Data were collected using a standardized survey form completed from patient medical records, covering sociodemographic, clinical, biological, and therapeutic information, including the type of maintenance treatment and hospitalisation history.

The variables studied concerned sociodemographic characteristics (age, sex, residence, education level, parents' education level); clinical and biological characteristics (age at diagnosis, circumstances of disease discovery, age at onset of first clinical signs, hemoglobin phenotype, average hemoglobin level (g/dL), average white blood cell count (G/L), average platelet count (G/L), urea, creatinine, transaminases, thick drop/blood smear, chest X-ray, abdominal ultrasound); treatments (during hospitalisation, at discharge); and clinical and outcome characteristics during follow-up (vaccination status, medical follow-up, treatment adherence, evolution under hydroxyurea, number of hospitalisations per year, common acute complications, and chronic complications). Treatment adherence was assessed from medical records, based on prescription refill logs and physician notes. Adherence was expressed as the percentage of doses taken relative to those prescribed over the last 6 months: Good adherence: ≥80% of doses taken, Poor adherence: <80% of doses taken.

Data entry was done using Excel 2019. The analysis involved calculating counts, means, and proportions. Categorical variables were compared using Fisher's exact test or the Chi-square test when applicable. Continuous variables were analyzed using the Student's t-test for normally distributed data. Statistical significance was set at $p < 0.05$. This study was conducted after obtaining authorization from the Medical and Scientific Director of Bouaké University Hospital. Anonymity and confidentiality were ensured by assigning an anonymization number to each survey form.

## 3. Results

### 3.1. Sociodemographic Characteristics

Out of a total of 272 sickle cell children in active follow-up, 81 had major sickle cell disease, and 45 met the inclusion criteria, representing 55%. They were male in 55% of cases, with a sex ratio of 1.25. The average age was 94.2 months, ranging from 8 to 180 months. Children aged ≥5 years accounted for 71% of cases, and the average age at diagnosis was 61.38 months. The children lived in Bouaké and were enrolled in school in 77.8% and 75.5% of cases, respectively (Table 1). According to the Expanded Program on Immunization (EPI), 88.9% of children were not up to date with their vaccinations. Vaccination coverage for EPI vaccines, according to the children's age, was 100%, while coverage for non-EPI vaccines was 12.5% each.

Table 1. Sociodemographic characteristics of children with major sickle cell disease (n = 45).

| Variable | Frequency | Percent |
|---|---|---|
| | Sex | |
| Female | 20 | 44.4 |
| Male | 25 | 55.6 |
| | Age | |
| 0 - 5 years | 13 | 29.0 |
| 5 - 10 years | 16 | 35.5 |
| 10 - 15 years | 16 | 35.5 |
| | Enrolled in School | |
| Yes | 34 | 75.6 |
| No | 11 | 24.4 |
| | Residence | |
| Bouaké | 35 | 77.8 |
| Outside Bouaké | 10 | 22.2 |

### 3.2. Clinical Characteristics

Severe anemia and arthralgia were the main presenting symptoms in 44.4% of cases. The children carried hemoglobin types SFA2, SC, and SS in 48.9%, 28.9%, and 22.2% of cases, respectively. They had an average hemoglobin level below 7 g/dL in 56% of cases. The mean hemoglobin was 7.15 g/dL, ranging from 5.7 to 12 g/dL. In 80% of cases, the white blood cell count was greater than 10,000 elements per $mm^3$ (Table 2). C-reactive protein (CRP) and thick blood smear tests were positive in 24.4% and 20% of cases, respectively. Imaging showed alveolar syndrome and acalculous cholecystitis in 22.2% and 2.2% of cases, respectively. The main diagnoses were infection, severe anemia, and vaso-occlusive crisis in 84%, 57%, and 44% of cases, respectively. One case of acute chest

syndrome was noted.

**Table 2.** Clinical characteristics of children with major sickle cell disease (n = 45).

| Variable | Frequency | Percent |
|---|---|---|
| Circumstance of Discovery | | |
| Severe anemia | 20 | 44.4 |
| Arthralgia | 20 | 44.4 |
| Jaundice | 17 | 37.3 |
| Hand-foot syndrome | 3 | 6.6 |
| Abdominal pain | 2 | 4.4 |
| Phenotype Type | | |
| SFA2 | 22 | 48.9 |
| SC | 13 | 28.9 |
| SS | 10 | 22.2 |
| Average Hemoglobin Level | | |
| <7 g/dL | 25 | 75.6 |
| 7 - 9 g/dL | 14 | 24.4 |
| ≥10 g/dL | 6 | 13 |
| Average White Blood Cell Count | | |
| >10,000 | 36 | 80 |
| 4000 - 10,000 | 9 | 20 |

### 3.3. Therapeutic and Outcome Characteristics

Treatment during hospitalisation consisted of antibiotic therapy and blood transfusion in 60% and 55% of cases, respectively. Children received a blood transfusion in 55.6% of cases. The outcome was favorable in 100% of cases. The combination of Hydroxyurea and Folic acid was prescribed in 24.4% of cases, and Ginkgo biloba + Folic acid in 75.6%. Good treatment adherence was observed in 64.4% (**Table 3**).

The children being followed had a number of hospitalisations ≥ 2 in 73.3% of cases. Children treated with the Ginkgo biloba + Folic acid combination had a number of hospitalisations ≥ 2 in 64.4% of cases versus 8.9% for those treated with the Hydroxyurea + Folic acid combination. Infection and anemia occurred in 84.4% and 57.7% of cases, respectively. Children treated with the Ginkgo biloba + Folic acid combination presented with infection-related complications in 64.4% of cases versus 20% for those treated with Hydroxyurea + Folic acid. Children treated with the Ginkgo biloba + Folic acid combination presented with anemia-related complications in 44.4% of cases versus 13.3% for those treated with Hydroxyurea + Folic acid. No chronic complications were observed during follow-up. The factor significantly associated with a lower number of hospitalisations was

treatment with hydroxyurea (p = 0.003) (Table 4).

**Table 3.** Therapeutic and Outcome Characteristics of Children with Major Sickle Cell Disease (n = 45).

| Variables | Frequency | Percent |
|---|---|---|
| Treatment during hospitalisation | | |
| Analgesic | 45 | 100 |
| Antibiotic | 27 | 60 |
| Blood transfusion | 25 | 55.6 |
| Antimalarial | 9 | 20 |
| Maintenance treatment | | |
| Hydroxyurea + Folic acid | 11 | 24.4 |
| Hydroxyurea + Folic acid | 16 | 35.5 |
| Adherence | | |
| Good | 29 | 64.4 |
| Poor | 16 | 35.5 |
| Number of hospitalisations | | |
| <2 | 12 | 26.7 |
| ≥2 | 33 | 73.3 |

**Table 4.** Factors associated with hospitalisation.

| Variables | Number of hospitalisations | | p |
|---|---|---|---|
| | <2 | ≥2 | |
| Age at Diagnosis | | | |
| <5 years | 8 | 14 | 0.18 |
| ≥5 years | 4 | 19 | |
| Phenotype | | | |
| SC (Sickle Cell trait) | 2 | 11 | 0.45 |
| SS + S$\beta$-thalassemia | 10 | 22 | |
| Parental Education | | | |
| No formal schooling | 2 | 12 | 0.29 |
| Received schooling | 10 | 21 | |
| Treatment Adherence | | | |
| Regular | 10 | 19 | 0.10 |
| Irregular | 2 | 14 | |
| Discharge Medication | | | |
| Hydroxyurea + Folic Acid | 7 | 4 | 0.003 |
| Tanakan + Folic Acid | 5 | 29 | |

## 4. Discussion

In order to improve the prognosis of children with major sickle cell disease followed in the pediatric department of Bouaké University Hospital, we conducted a retrospective, analytical, single-center study aimed at describing their morbidity. Due to the retrospective nature of the study, some clinical and follow-up data were partially missing from the medical records. To address this limitation, phone calls were made to complete the information with the families concerned. Despite this methodological limitation, the results obtained allow us to highlight the following discussion points.

From a sociodemographic perspective, data analysis reveals a male predominance in the study, with a sex ratio of 1.25. This result is close to that reported by Kouadio in 2022 in the same department (sex ratio: 1.3) [8] and corroborated by Bianga *et al.* [9]. However, Yabo in Bamako, Mali, observed a female predominance with a sex ratio of 0.86 [10]. This disparity between studies reflects the autosomal recessive, non-sex-linked nature of sickle cell disease, where sex distribution remains statistically random. Regarding the age of the children, 71% were older than 60 months, with a mean age of 94.2 months [range: 8 - 180 months]. This trend is comparable to that described by Kouadio (mean: 87 months; range: 11 - 192 months), although his cohort included a majority of children under 5 years (54%) [8]. Yabo [10] found 60% of children aged 0 to 59 months. Marquez [11] reports a predominance (46%) of children over 10 years old, indicating a slightly different inclusion profile.

The average age at diagnosis remains concerning, at 61.38 months in this study, indicating late detection. This finding is similar to results from Yabo (mean age: 5.11 ± 3.14 years) [10] and Seck *et al.* in Senegal (mean age: 4 years 10 months; range: 1 month - 17 years 7 months) [12]. This diagnostic delay is due to the absence of a neonatal screening program and a general lack of awareness of the disease among families. In our setting, the diagnosis is typically made after the first clinical crises. Offering free hemoglobin electrophoresis for pregnant women in Côte d'Ivoire would be a relevant strategy to improve early detection.

The study revealed insufficient vaccination coverage outside of the Expanded Program on Immunization (EPI), with only 12.5% of children up to date. This low coverage may be due to the high cost of vaccines, which is often unaffordable for some families. However, adhering to the vaccination schedule is crucial for children with sickle cell disease, who are particularly vulnerable to infections. These infections, combined with inadequate hygiene and lifestyle practices, promote hemolytic episodes and vaso-occlusive crises.

The circumstances of disease discovery were dominated by severe anemia and joint pain (44.4% each). These initial signs are similar to those reported by Seck *et al.*, who identified vaso-occlusive crises (58.5%) and anemia (21.1%) as the main reasons for consultation [12]. In Africa, diagnosis is often made following symptoms such as VOCs, jaundice, splenomegaly, or chronic anemia [10]. Before the age of 6 months, these manifestations are rare, which contributes to diagnostic

delays.

The acute complications observed in our study were dominated by infections (84.4%) and anemia (57.8%). These results are comparable to those from Yabo (infection: 66%, anemia: 46%) [10]. These two complications represent a major part of pediatric morbidity related to sickle cell disease and account for high lethality in resource-limited countries.

Severe anemia raises concerns about blood availability. The mean hemoglobin level was 7 g/dL in 56% of cases. The overall average was 7.15 g/dL, with a range of 5.7 to 12 g/dL. This result is comparable to Yabo's [10] who reported a mean hemoglobin level of 7.9 g/dL, with a minimum of 5 g/dL and a maximum of 11.2 g/dL. This average has also been observed in other African studies, such as that by Elie *et al.* [13].

Therapeutically, all children were prescribed folic acid at hospital discharge. Hydroxyurea was prescribed in 24.4% of cases, and Ginkgo biloba in 75.6%.

The study shows that after 12 months of follow-up, children with major sickle cell disease experienced fewer complications and hospitalisations when treated with Hydroxyurea + Folic acid compared to those treated with Ginkgo biloba + Folic acid. Thus, the treatment with Hydroxyurea combined with Folic acid was the factor significantly associated with a lower number of hospitalisations. This result demonstrates the superiority of Hydroxyurea in reducing complications and hospitalisations in children with major sickle cell disease compared to vasodilators. This superiority may be due to Hydroxyurea's ability to increase fetal hemoglobin (Hb F) expression. Higher levels of Hb F inhibit the polymerization of Hb S during the sickling process, leading to reduced vaso-occlusive and hemolytic complications [14].

Furthermore, Hydroxyurea increases hemoglobin levels, mean corpuscular volume, and red blood cell hydration, thereby reducing the risk of chronic anemia [15] [16]. Hence the importance of early initiation of Hydroxyurea therapy for all symptomatic SS and S/$\beta^{\circ}$ thalassemic children from the age of 2 years, according to French National Authority for Health 2024 recommendations [17]. These results support the reinforcement of the local pediatric sickle cell disease management protocol at Bouaké University Hospital, particularly through systematic early initiation of hydroxyurea in eligible children, regular monitoring of treatment adherence, and improved access to non-EPI vaccines to reduce infection-related morbidity.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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