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# Hemoglobinopathies during Severe Anemia in African Pediatric Hospital

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**Abstract**

*The common clinical picture of hemoglobinopathies is chronic hemolytic anemia of varying intensity according to the type of hemoglobin abnormality. It can be decompensated into severe acute anemia during an acute morbid state. Côte d'Ivoire is part of the sicklemic belt. Sickle cell disease is a public health issue.*

*The general objective was to describe the profile of hemoglobinopathies of children from 6 months to 15 years old in hospital. We conducted a descriptive and analytic cross-sectional study in children aged 6 months to 15 years hospitalized with severe anemia for 8 months in 2016. We conducted a descriptive and analytical cross-sectional study on children from 6 months to 15 years hospitalized for severe anemia for 8 months in 2016. The CHI 2 test was used to determine the relationship between the presence of hemoglobinopathy and certain clinical and paraclinical variables. The observed difference was statistically significant when p was <0.05.*

*The prevalence of hemoglobinopathies was 19.8%. The 3 main types of hemoglobinopathies identified included AC hemoglobin (34.2%), composite heterozygosity S / ß thalassemia or SFA2 (18.4%) and an equal proportion of SS homozygous sickle cell disease (15.8%) and β-Thalassemia minor (15.8%). Severe malaria was diagnosed in 87% of cases and 3 patients had complications related to hemoglobinopathy at admission. Stunting and positive malaria tests were significantly greater in hemoglobinopaths.*

*The average age of screening was 2.9 years. The top 3 types of hemoglobinopathies identified included hemoglobinosis AC (34.2%), composite heterozygotia S/ß thalassemia or SFA2 (18.4%) and equal proportion SS homozygous sickle cell disease (15.8%) and β-minor thalassemia (15.8%). The prevalence of hemoglobinopathies was 19.8*

*The interest of the study is screening of carriers early, including neonatal screening or a subsidy for hemoglobin electrophoresis.*

**Keywords:** *hemoglobinopathies, severe anemia, child hospitalized, Côte d'Ivoire*

## Introduction

The common clinical picture of hemoglobinopathies is chronic hemolytic anemia of varying intensity according to the type of hemoglobin abnormality **[1]**. In Africa, sickle cell disease is a real public health issue. It is the most common hemoglobinopathies in the Siklemic zone of which Côte d'Ivoire is part. The prevalence's are highest and the natural evolution is strewn with chronic and acute complications, sometimes fatal, including anemia **[2;3;4; 5]**.

Indeed, in the case of acute morbidity state, generally infectious, chronic anemia may decompensate in severe acute anemia **[3; 4; 5]**. This situation requires urgent hospital care **[6; 7; 8]**. In Côte d'Ivoire, malaria infection in its severe form is most often mentioned. However, the involvement of hemoglobinopathies is under-reported. Neonatal screening is not done. Performing hemoglobin electrophoresis remains

limited by certain obstacles: the low attendance rate of maternal-child health services, the low socio-economic level and the lack of medical coverage for the majority of the population frequenting public structures, the lack of the technical platform in these health centers **[9]**. Updated data on sickle cell disease in pediatric settings are not available. The latest prevalence estimates made by Cabane and Sangaré go back several decades **[4; 6].**

The general objective was therefore to describe the profile of hemoglobinopathies in children from 6 months to 15 years in hospital. It specifically involved identifying clinical features, analyzing electrophoretic profiling of the study population and disturbances observed at the hemogram.

## Equipment and methods

### Type of study

It was a cross-sectional descriptive and analytical study in children aged 6 months to 15 years hospitalized for severe anemia.

### Framework and period of study

Our study took place from January 15th to August 31st, 2016 for 8 months in the pediatric medical departments and the hematology unit of the central laboratory of the Yopougon University Hospital.

### Sampling method and sample

As the overall prevalence of hemoglobinopathies is unknown, the minimum size of the study sample was calculated based on the prevalence of sickle cell disease in the Ivorian population. The last available estimate of this prevalence is 13% in 1970**. [4,10,11**]. We then applied the formula of the prevalence study that is

N = ε2 p q / d2, with N = minimum sample size ε = 1.96 for α = 5%, p = 12%, q = 1-p = 88%, d = precision set at 5%. N=192 people at least to be included in our study.

### Criteria for inclusion

The study included children aged 06 months to 15 years hospitalized for severe anemia and having performed hemoglobin electrophoresis during hospitalization.

### Criteria for non-inclusion

We did not include children previously followed for hemoglobinopathies and/or those who were transfused with globular cup within three (03) months prior to hospitalization.

## Course of the study

### Parental consent

The patients were enrolled as and when admitted to hospital. Legal guardians have given prior informed consent. The data was collected on a survey sheet with an anonymity number. The physical examination revealed a clinical anemia with or without signs of seriousness, and assessed the nutritional state of the children, the weighing and the size measurement. The data obtained was compared to the 2006 WHO growth standards. Systematic venous blood collection was performed in an EDTA tube. Hemoglobin electrophoresis was prior performed with an hemogram.

Iron metabolism was performed only on patients with SFA2 or SSFA2 hemoglobin, microcytic hypochromic anemia and Hb S > 80% **[1]**. Additional paraclinical examinations were prescribed according to the clinical context. These included a thick drop or TOR of malaria, blood culture, lumbar puncture of urinary cytobacteriological examination (ECBU), radiographic explorations. A specific care proposal in the clinical hematology department was made to patients screened with a hemoglobin abnormality.

## Data collection

The data was collected on a standardized survey form. This sheet included information on epidemiological, clinical and paraclinical characteristics, etiological diagnosis and management.

### Operational definition of terms [3;12]

We considered as:

- Severe anemia: clinical anemia with signs of intolerance and / or hemoglobin rate < 5 g / dl

- Non-severe anemia: hemoglobin levels > 5 g/dl with no signs of severity and intolerance.

- Moderate acute malnutrition: any child over 6 months of age whose Z weight / height (P / T) score is in the range [-3 -2 [, with or without a mid-upper arm circumference (MUAC) included in the interval [11.5 cm 125 cm [, without edema of the bilateral lower limbs.

- Severe acute malnutrition: any child over 6 months of age with a Z Score P / T <-3, with or without a BP <11.5 cm with or without bilateral lower limb edema. It may be an infant under 6 months old or weighing less than 3 kg with severe breastfeeding difficulties and / or not taking weight at home and / or the Z Score P / T <-3 with or without bilateral edema.

- Stunting: any child under 5 years old whose Z size/ age score (T/A) <-2

## Statistical analysis

The data collected was captured and analyzed using Epi Info 7 software. The descriptive analysis method was done by determining averages and proportions. Concerning the analytical statistical analysis, the CHI 2 test was used to determine the relationship between the presence of hemoglobinopathie and certain variables (nutritional status, growth, malaria tests, severe malaria form, and hemoglobin at admission). The observed difference was statistically significant when p was <0.05.

## Results

### Descriptive study

We enrolled 192 patients including 122 boys and 70 girls; the sex ratio was 1.74 in the sample and 1.2 in hemoglobinopaths. Children under 5 accounted for 82.3% of the sample. The average age of children with a hemoglobin abnormality was 2.9 months, with a minimum of 6 months and a maximum of 13 years. Clinically, history revealed an incomplete vaccination schedule in 52% of cases, a use of long-lasting insecticidal insecticide-treated bednet (LLIN) in 45% of cases, at least one previous hospitalization for 36% of children, of which 14 (38.8%) were transfused at least once.

The conclusions of the clinical examination on admission are compiled in Table I. Hemolytic and painful syndromes were present in 110 (42%) and 12 (6%) children respectively. In addition, 19.3% of the patients were stunted and 30.7% were acutely malnourished.

**Table I.** *Distribution of patients by clinical signs at admission*

| Clinical examination | Frequency | Percentage **(%)** |
|---|---|---|
| Functional signs | | |
| Fever | 192 | 100 |
| Painful syndrome | 12 | 6 |
| Physical Signs | | |
| Decompensated anemia | 192 | 100 |
| Hemolytic syndrome | | |
| - Splenomegaly | 56 | 29,1 |
| - Hemoglobinuria | 34 | 17,7 |
| - Hepatomegaly | 14 | 7,3 |
| - Ictera | 6 | 3,1 |
| Malnutrition | | |
| - Acute malnutrition | 59 | 30,7 |
| - Stunting | 37 | 19,3 |
| Coma | 26 | 13,5 |
| Meningeal Syndrome | 2 | 1 |

Systematic hemoglobin electrophoresis allowed us to detect an hemoglobinopathies in 38 patients, representing a prevalence of 19.8% of the sample. The 3 main types of hemoglobinopathies identified included AC hemoglobin (34.2%), composite heterozygosity S / ß thalassemia or SFA2 (18.4%) and an equal proportion of SS homozygous sickle cell disease (15.8%) and β-Thalassemia minor (15.8%).

The electrophoretic profile is recorded in Table II.

**Table 2.** *Distribution of patients according to hemoglobin profile*

| Type of Hemoglobin | | Size **(n=192)** | **Proportion (%)** |
|---|---|---|---|
| Normal hemoglobin | | **154** | **80,2** |
| Symptomatic forms | | | |
| Hemoglobinopathy | SFA2 | 7 | 18,4 |
| | SSFA2 | 6 | 15,8 |
| | Intermediate β-thalassemia | 2 | 5,2 |
| | Sickle cell SC | 1 | 2,6 |
| **Non symptomatic forms** | | | |
| Hemoglobinopathy | Trait AC | 13 | 34,2 |
| | β-Thalassémie mineure ou PHHF* | 6 | 15,8 |
| | Line AS | 3 | 8 |

HPFH * = Hereditary Persistence of Fetal Hemoglobin.

These abnormalities of hemoglobin were variously associated with other morbid states diagnosed after the completion of the other para-clinical assessments. The three main pathologies were severe malaria (87%), common germ pneumonia (11.5%) and acute pyelonephritis (5.7%). The predominant forms of severe malaria were the anemic form (56.9%), the neurological form (15.8%) and the neurological and anemic forms (15.3%).

An hemoglobinopathy was associated in 28, 2 and 3 cases, respectively. In addition, we noticed 3 children under 5, hemoglobinopaths who had an infectious complication upon admission; these included osteoarthritis (SFA2), splenic abscess (B-Thalassemia intermediate) and cholecystitis (SSFA2). Concerning the results of the hemographs, the average of some admission parameters is reported in Table III. The mean hemoglobin level was 4.91 g / dl with hypochromia (24 µg) and microcytosis (73.56 µl). The extreme values were 1.70 g / dl and 7.90 g / dl.

**Table 3.** *Mean values of white blood cells, hemoglobin and platelets at the hemogram of the study population at admission*

| Parameters | Average | Minimum | Maximum |
|---|---|---|---|
| White blood cells | 18 184,18 | 4 000 | 168 000 |
| Neutrophil polynuclear cells | 50,39 | 3,80 | 87,50 |
| Lymphocytes | 40,29 | 6,10 | 74,80 |
| Hemoglobin | 4,91 | 1,70 | 7,90 |
| Hematocrit | 15,19 | 5,50 | 28,10 |
| MCV | 73,56 | 48,60 | 113,70 |
| MCH | 24,02 | 12,50 | 32,60 |
| CCMH | 32,52 | 17,90 | 45,20 |
| Platelets | 183 963,48 | 8 300 | 806 000 |

## Analytical study

It showed a statistically significant link between hemoglobinopathy and some abnormalities. The analysis in Table IV reveals that there are: stunting (p=0.002), positivity of malaria tests (p=0.007). There is no statistically significant difference between hemoglobin abnormalities and the occurrence of severe forms of malaria (p=0.8).

**Table 4.** *Influence of Haemoglobinopathie on Clinical and Biological Parameters*

| Sanitary abnormalities | Hemoglobinopathie | | Absence of hemoglobinopathie | | P |
|---|---|---|---|---|---|
| | $n_1$ | % | $n_2$ | % | |
| Acute malnutrition | 15 | 39,47 | 44 | 28,57 | 0,192 |
| Stunting | 14 | 36,84 | 23 | 14,93 | 0,002 |
| Positive malaria test | 28 | 73,68 | 139 | 90,26 | 0,007 |
| Hb < 5g/dl | 13 | 34,21 | 83 | 53,90 | 0,0534 |
| Severe malaria anemic form and other complications | 12 | 42,86 | 56 | 40,29 | 0,8 |

## Discussion

Limitations of the study

We encountered some difficulties in the course of the investigation. This was mainly due to the non permanent realization of hemoglobin electrophoresis by the laboratory of the hospital structure and the long delay of the rendering of the results

The results of the study concern 192 children admitted for severe anemia. The prevalence of hemoglobinopathie is 19.8% higher than that of the general population (12%) **[13]**. It would be linked to a selection bias. We had a heterogeneous electrophoretic profile. AC hemoglobin is the major hemoglobin abnormality in our investigation. It is usually asymptomatic, unlike homozygous sickle cell disease and β-thalasso sickle cell disease major responsible for anemic and / or vaso-occlusive seizures through at least one favorable factor, including impaludation **[2]**. These forms, even outside the seizures, have a continuous haemolysis of the red blood cells **[14]**.

The most frequently observed clinical signs indicate isolated hemolytic anemia, as well as the complications

observed at admission are those that are expected and in the literature. The presence of fever indicates an infectious disease as a decompensation factor for chronic hemolytic anemia **[15]**. Indeed, 87% of hemoglobinopathic subjects had severe malaria. The involvement of malaria is particularly described for sickle cell disease in the literature [internet document] and is controversial **[15;16]**. Our observations concerning the positivity of malaria tests are consistent with some authors who assert that the evolution of parasitaemia of sickle cell is comparable to that of the normal subject **[15;17]**.

Others, on the other hand, consider that malaria infection occurs in the AS subject as in the AA normal subject, but the parasite density is much lower and the grave clinical forms less frequent. However, the protective effect in the AS heterozygote disappears in the period of appearance of anti-malaria immunity. However, the protective effect of HbS on malaria is inconsistent **[17]**.

Patients with major sickle cell disease are not protected from malaria compared to AS subjects, but exposed in the same way as non-sickle cell patients **[17]**.

Could the fact that we did not find a statistically significant link between the clinical form of malaria and hemoglobinopathy be related to the presence and prevalence of other abnormal hemoglobins?

The previous indication of transfusion for some of them (14.1%) should have been an opportunity to screen for hemoglobinopathy, especially since Côte d'Ivoire belongs to the sickle cell belt. This could be due to a lack of financial means because this review is not subsidized by the state. This situation may justify the average age of 2.9 years of late screening. It shows the interest of neonatal screening **[18]**.

The hematological disorders observed vary according to the degree of the deficit. They are discrete in heterozygous subjects but still very serious in the homozygote **[19]**.

Anemia of varying intensity, microcytic hypochromic is very often reported in the literature **[15;17;19]**. The rate of hemoglobin in the study is lower than that observed in Europeans. This difference could be explained by the influence of environmental and social economic factors **[17]**.

The microcytosis observed in some hemoglobin opathies patients willingly guides us towards the association with an underlying iron deficiency.

In Côte d'Ivoire, chronic malnutrition is the most common form of malnutrition among children from 0 to 59 months **[12,13]**.

The worsening of anemia would be due to underlying iron-deficiency anemia resulting from a deficiency of dietary intake that does not meet the nutritional needs related to growth **[6]**. In addition, repeated infections expose sick patients to many risks including stunting **[6]**. Hemoglobinopathies are inflammatory diseases, among which one marker is leukocytosis **[20;21]**. The average number of white blood cells, meanwhile, translates an almost constant leukocytosis. About the average number of platelets in our study, it corroborates that reported in the literature **[20]**. It has been shown that activated platelets secrete thrombospondin (TSP) involved in the occurrence of hypercoagulability, which is responsible for the onset of sickle cell seizures **[21]**.

## Conclusion

This work enabled us to detect hemoglobinopathies in pediatric hospitals in children under 5 with severe anemia. Among them, we diagnosed a significant number of infectious complications. The interest of the study is the screening of carriers early, including neonatal screening or a subsidy of hemoglobin electrophoresis, adequate and multidisciplinary follow-up including the pediatrician, the pediatric surgeon, the orthopedist and the nutritionist.

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