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# Neonatal Screening of Sickle Cell Disease at the Centre Hospitalier Universitaire de Libreville: Epidemiological and Clinical Aspects

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## Abstract

**Introduction:** Sickle cell disease is the most common genetic disease in the world. Neonatal screening is not widespread in Gabon. The interest of a diagnosis from birth allows early management of the disease and prognosis improvement.

**Objective:** To determine the frequency of sickle cell trait and its different forms, to identify factors associated with risks of major sickle cell syndrome.

**Patients and Methods:** A transversal pilot study was carried out between 13th November and 25th December 2014 at the Centre Hospitalier Universitaire de Libreville. Only newborns of consenting mothers were included. The variables studied were socio-demographic data, obstetrical history, mode of delivery and maternal and newborn electrophoretic status, anthropometric parameters, Apgar score and hemoglobin electrophoresis result. The statistical analyses were performed using Microsoft Excel software.

**Results:** 202 newborns from 197 mothers were selected, including 5 pairs of twins. Majority of mothers were Gabonese (91,8%); The 20 - 30 age group represented 67.0% with an mean age of 26 years old, extreme 14 and 45. Primiparous women represented 60.9% of the studied population. Delivery was vaginal in 187 cases (78.17%). Maternal hemoglobin status was known for 118 women (59.9%) and revealed AA profile in 96 cases (81.4%). Full term infants were 187 (94.9%); 115 newborns were male (56.9%). Average weight was 3100 grams, extreme 1690 and 4500 grams. The newborns electrophoretic profile was of type AA in 158 cases (78.2%). The AS heterozygous type was identified in 42 cases (20.8%) and major sickle cell syndrome in 2 cases (1.0%).

**Conclusion:** High prevalence of morbidity and mortality in case of sickle cell disease is well known. Neonatal screening, an effective tool for detecting this condition, must be systematic and allow for early management.

***Keywords:*** *Sickle Cell Disease; Neonatal Screening; Major Sickle Cell Syndrome*

## Introduction

Sickle cell disease is a genetic disorder caused by a point mutation and inherited in an autosomal recessive mode. Abnormal hemoglobin S in red blood cells causes deformations of red blood cells into sickle or sickle-shaped [1]. Sickle cell disease or major sickle cell

syndrome (MDS) includes homozygous, double heterozygous or composite heterozygous forms. These forms present with varied clinical manifestations and severity of disease [2,3]. Sickle cell disease, ranked 4th among the World Health Organization's (WHO) public health priorities, is a public health problem in most African countries. According to this organization, about 5% of the world's population has sickle cell trait with high prevalence in Black Africa [4]. Every year, about 300,000 to 500,000 children are born with sickle cell disease, more than 200,000 of them in Africa and half of them will die before the age of 5 [4- 6]. In the first weeks of life, sickle cell children show no signs of the disease; complications appear around the third month [7]. In developed countries, progress has been made in the management of sickle cell disease through early detection. Studies have shown that the incidence of complications in sickle cell children can be reduced by introducing neonatal screening to provide them with access to effective treatment that would change the course of disease morbidity and mortality [8].

In Gabon, the disease affects about 2% of the general population; systematic screening is not common practice and diagnosis is made only when serious complications occur. Previous studies have reported a prevalence of 21.1% of sickle cell trait in children over 15 years old and prevalence of 1.8% disease in newborns [9,10]. Early disease management, late diagnosis and impact stress the need for a systematic neonatal screening. The objective of this study was to determine the prevalence of sickle cell trait and to identify the different types of sickle cell disorders and the characteristics of Major Sickle Cell Syndrome, in newborns at the Centre Hospitalier Universitaire de Libreville (CHUL).

## Patients and Methods

This was a transversal, descriptive, analytical and prospective pilot study carried out between November 13th and December 25th, 2014, within the Maternity Unit of the University Hospital Centre of Libreville. Newborns whose mothers consented were included. Data were collected through a pre-designed personnal form. Studied variables for newborn were: gestational age, sex, birth weight (g) and results of hemoglobin electrophoresis; for mothers, nationality, age, parity and results of hemoglobin electrophoresis were the parameters of interest. Blood samples were taken in the newborn at 72 hours of life by heel capillary sampling, sterile lancet puncture at the rim, after massage and disinfection using a 70-degree alcohol swab. Blood drops were collected on blotting paper by direct contact at rate of 2 to 4 discs per blotting paper and per newborn. The blotting papers were dried in open air and placed in an envelope stored at +4° Celsius before being transferred for analysis to the laboratory of Centre International de Recherche Médicale de Franceville (CIRMF). For each newborn, the blotting paper included information on the mother's first and last name and the same sample identification number as in the personnal form was applied. Isoelectrofocusing onagarose gel support was the analytical technique [11]. Test results discriminated between the normal hemoglobin AA electrophoretic profile, the asymptomatic AS or AC heterozygous form, the SS homozygous form and the SC composite heterozygous form [12]. Results were sent to the Service in charge responsible for informing the families. Children screened for a genotype associated with MSCS were referred to the outpatient unit for more accurate information to parents for follow-up. Statistical analyses were performed using Microsoft Excel software version 7 Windows for calculating percentages and averages. Prism 5 software, version 4.0, for determining the frequency of hemoglobin status and calculating $Chi^2$.

## Results

From 470 recorded live births, 202 newborns from 197 mothers were included, thus achieving a coverage rate of 43%. Five children were the result of twin pregnancies. Gabonese infants accounted for 91.8% of the population and other Central and West African countries for 8.2%. Republic of Congo, Cameroon and Equatorial Guinea represented 4.1% of all parturient women; Ivory Coast, Mali, Togo, Nigeria and Burkina-Faso accounted for another 4.1%. Mothers were on average 26 years old, with extremes of 14 and 45. The 20 to 30 age group accounted for 67.0% whereas 21.3% of mothers had over 30 years, and 11.7% had under 20 years. Primiparous women accounted for 60.9%, multiparous women for 37.1% and large multiparous women for 2.0%. Delivery was vaginal in 78.1% cases and cesarean in 21.8%. The hemoglobin status of 59.9% of mothers was known, while that of fathers was unknown in all cases. AS electrophoretic profile was identified in 18.6% of cases while AA profile was identified in 81.4% of cases. No mothers had major sickle cell syndrome (Table 1).

Among newborns, 43.1% were male and 56.9% female, thus a sex ratio of 0.75. Large majority of deliveries (91.9%) were at term, compared to 5.1% for near-term deliveries and 3.0% were post-terms. Birth weight was normal in 94.0% of cases and 5.9% had less than 2500 g. Abnormal hemoglobin was identified in 21.8% of newborns. Their mothers came from West African countries in two cases (Burkina Faso; Togo) and three came from Cameroon. Heterozygous profile was observed for 20.8% newborns, including 18.9% for AS type and 1.9% for AC type. Major sickle cell syndrome was reported for 1% of births, including 0.5% for SC composite heterozygous type and 0.5% for SS homozygous type. Hemoglobin C was reported in 2.4% of cases (Table 2).

## Discussion

The average coverage rate is low compared to 56.0% reported in the Democratic Republic of Congo. This low rate is attributable to lack of mothers' participation, newborns being transferred to other health facilities, lost of view of children sent to maternity hospitals and the non-inclusion of very premature infants, where frequent reporting of false positives makes it difficult to analyse [12].

The mothers were relatively young and the majority were primiparous. In Gabon, fertility rate, young age of mothers, absence of compulsory prenuptial check-ups increase the risk to have more children with sickle cell trait or disease [14]. The rate of parturient women being aware of their electrophoretic status is comparable to the 58.9% rate reported in Cameroon and lower than the 71% rate in Nigeria. In case of fathers, the awareness of their electrophoretic status was high compared to Cameroon, which reported 9.6% rate [15,16]. The request for testing is systematic in pregnancy follow-up, but cases of positivity are not followed by screening of the spouse or information

| Maternal Parametres | n (197) | % |
|---|---|---|
| **Nationality** | | |
| Gabonese | 181 | 91,9 |
| Non gabonese | 16 | 8,1 |
| West African Countries | 8 | 4,0 |
| Other Central African countries | 8 | 4,0 |
| **Age (ans)** | | |
| < 20 | 23 | 11,7 |
| 20 - 29 | 132 | 67,0 |
| ≥ 30 | 42 | 21,3 |
| **Parity** | | |
| Primiparous | 121 | 59,9 |
| Multiparous (2-5) | 73 | 37,2 |
| Large multiparous (> 6) | 4 | 2,0 |
| **Mode of delivery** | | |
| Vaginal (normal) | 152 | 77,2 |
| Vaginal (dystocic) | 2 | 1,0 |
| Caesarian | 43 | 21,8 |
| **Electrophoretic profile (n = 118)** | | |
| AA | 96 | 81,4 |
| AS | 22 | 18,2 |

***Table 1:*** *Distribution of mothers by characteristics and electrophoretic profile.*

| Neonatal Parametres | n (202) | % |
|---|---|---|
| **Birth term (Weeks of gestation)** | | |
| 33 to 36+6 days (preterm or near-term) | 10 | 5,0 |
| 37 à 41+6 days (at term) | 187 | 92,5 |
| ≥ 42 (post-term) | 5 | 2,5 |
| **Birth weight (g)** | | |
| < 2500 | 12 | 6,0 |
| ≥ 2500 | 190 | 94,0 |
| **Gender** | | |
| Male | 87 | 43,1 |
| Female | 115 | 56,9 |
| **Electrophoretic profile** | | |
| AA | 158 | 78,2 |
| AS | 38 | 18,8 |
| AC | 4 | 1,9 |
| SC (MSCS) | 1 | 0,5 |
| SS (MSCS) | 1 | 0,5 |

***Table 2:*** *Distribution of newborns by characteristics and electrophoretic profile.*
*MSCS: Major Sickle Cell Syndrome.*

to the couple for early screening of the child. This is of concern and reinforces the need for educational programmes for health professionals and families to screen newborn siblings. The rate of mothers with sickle cell trait was comparable to the 15.3% rate in Cameroon and no mothers were found to be suffering of MSCS, unlike that study which reported two SS sickle cell mothers [16]. The mothers were from countries where the prevalence rate of sickle cell trait is high; 16.1% in Togo, 25.5% in Burkina Faso 25% to 30% in Cameroon [17-19]. Proportion of mothers with sickle cell trait is higher in West African countries than the 1.7% rate recorded in the Democratic Republic of Congo [20]. Births were eutocic, vaginal and most babies were born at term with normal birth weight. These findings confirm other studies in the literature asserting that mothers with AS electrophoretic type do not have more complications when giving birth than those with AA electrophoretic type and that newborns with sickle cell trait or major sickle cell syndrome do not have any consequent pathology at birth. A study in Cameroon found no statistically significant difference between the anthropometric parameters of infants carrying the sickle cell gene and those with normal electrophoresis results, except for the head circumference, which tends to be smaller in newborns with S haemoglobin [21]. The predominance of females among newborns diagnosed with abnormal hemoglobin reported in the Cameroon study, where 54.0% of children with Major Sickle Cell Syndrome were female and 45.95% were male. In Gabon, a survey in 2007 reported a male prevalence of 45.3% for heterozygous AS type and 5.6% for homozygous SS type [10,16]. Other authors do not find any predominance between the two genders. Sickle cell disease being a genetic disease not related to gender, these differences are thus in accordance with the epidemiological data of each country [22]. The prevalence of AS sickle cell trait is consistent with the 15.1% prevalence reported in Gabon in 2007 and with the 16.9% rate in the Democratic Republic of Congo [10,16]. This is higher than the 7.9% rate reported in Senegal, 9.9% in Mali and 13.2% in Cameroon [17,21,24]. High rate can be explained by poor sampling and the sickle cell trait providing resistance to Plasmodium falciparum malaria in endemic areas such as Gabon [24]. The prevalence of Major Sickle Cell Syndrome was lower than the 1.9% rate reported in Gabon in 2007; 1.4% in the Democratic Republic of Congo and 2.8% in Nigeria [10,16,18]. Homozygous SS type rate of 0.6% in Cameroon was similar to our study [17]. Such a profile is most common in Central Africa

and the reported low rate may be in accordance with the sample size and uni-centricity of the study [25]. The frequency of abnormal C hemoglobin is high in West African countries where its prevalence is 15.0% and low in Central Africa [26]. Its prevalence was higher than that 0.22% rate observed in the Great Lakes region [27]. The reported rates of SC heterozygous composite and AC heterozygous forms are comparable to the respectively 0.2% and 1.1% rates in Nigeria.

Frequencies of 0.4% for SC forms and 5.6% for AC forms were found in Mali. These rates were much lower in Gabon in 2007 with 0.84% for AC forms and 0.1% for SC forms [10,18,27]. Presence of C hemoglobinosis in Gabon may be attributed to its population being highly mixed with peoples of diverse origins and crossbreeding, and consequently the occurrence of different genetic components of sickle cell disease [9,28].

## Conclusion

The frequency of sickle cell trait remains a concern and the detection of Major Sickle Cell Syndrome is a reminder that sickle cell disease remains a neglected disease in Gabon. Early management, consequences of the disease and late diagnosis justify the importance of systematic neonatal screenings. Implementation of a national programme focusing on a cost-efficient screening approach would allow detection of genetic forms of the disease combined with a prevention strategy that would reduce morbidity and mortality associated with this condition.

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