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Maternal Haemoglobinopathy and Neonatal Morbidity and Mortality in a Reference Center in Abidjan

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Abstract

Introduction: Sickle cell disease is the most common hemoglobinopathy in the world. In Côte d'Ivoire, newborn screening is not yet popular. The objective was to describe the profile of newborns of hemoglobinopathic mothers hospitalized in the paediatrics department of the Cocody University Hospital. **Population and method:** This was a cross-sectional and analytical study that took place over a period of 2 years (November 2017-November 2019). Two hundred and fifty newborns whose mothers were carriers of a hemoglobin abnormality were included in the study. **Results:** The mean age of the mothers was 28.99 years; they had major sickle cell disease in 14% of cases (SS: 7 cases; SC: 17 cases; SAFA2; 8 cases; SFA2: 4 cases). The sickle cell trait AS was present in 49.5% of cases and hemoglobinosis C appeared only in the heterozygous AC form (36.5%). Low birth weight ($p = 0.046$), hypotrophy ($p = 0.08$), and bacterial infection ($p = 0.009$) were more common in newborns born to mothers who were carriers of a major form. Mortality was 14.8% and the causes of death were hypoxic and ischemic encephalopathy (35%), Neonatal Bacterial Infection (16%) and prematurity (24%). **Conclusion:** Newborns of mothers with hemoglobinopathies are at risk. The introduction of newborn screening would improve their care.

Keywords

Mother's Haemoglobinopathy, Newborn, Morbidity and Mortality

1. Introduction

Hemoglobinopathies are genetic disorders of haemoglobin, with autosomal recessive inheritance affecting the protein fraction of haemoglobin. There are two types of hemoglobinopathies: hemoglobinoses and thalassemias. Sickle cell hemoglobinosis or sickle cell disease is the most widespread. According to the World Health Organization (WHO), 5% of the world's population is a carrier of a sickle cell mutation and 240,000 newborns with sickle cell disease are born each year worldwide. Similarly, nearly 7% of pregnant women are thought to be carriers of hemoglobinosis or thalassemia [1].

In Côte d'Ivoire, data on the prevalence of sickle cell disease are outdated [2]. Since 2022, the country has had a national strategic plan to control sickle cell disease, focusing on early screening, particularly neonatal screening, early treatment using innovative new therapeutic protocols, and capacity-building for medical staff. However, diagnostic facilities are still inadequate, especially in rural areas, and neonatal screening is in the pilot phase in a few level III referral facilities. This screening allows appropriate management of newborns born to mothers suffering from hemoglobinopathies. In fact, the association of sickle cell disease and pregnancy is a haunting for the medical team because it is often punctuated by complications in the mother and the fetus [3] [4]. By initiating this study, we have set ourselves the general objective of contributing to improving the quality of care for newborns of hemoglobinopathic mothers. Specifically, the aim was to describe the characteristics of mothers and their newborns, to describe the morbidity, to determine the neonatal mortality rates and identify causes of death, describe the profile of newborns born to mothers with sickle cell disease.

2. Population and Method

We carried out a cross-sectional study with analytical purposes that took place over a period of 2 years (November 2017-November 2019) in the neonatal block of the Cocody University Hospital in Abidjan. All medical records of newborns whose mothers were carriers of a hemoglobin abnormality were included in the study. Unusable files (incomplete, incorrectly filled in or not containing hemoglobin electrophoresis) and not found were not retained.

Data collection and analysis: Data were retrospectively collected from hospitalization registers, medical records and a pre-established survey form for each file. The variables studied were as follows.

For mothers: age, occupation, gynaecological-obstetric history (spontaneous abortion, stillbirth, pregnancy, pregnancy, parity, prenatal consultation and check-up, complications during pregnancy), type of pregnancy, hemoglobin electrophoresis profile.

For newborns: sex, mode of delivery, age at admission, place of origin, clinical characteristics (gestational age, anthropometric measurements, Apgar score at the 5th minute, reason for admission and physical signs, diagnosis retained), and biological characteristics (CBC, CRP, Blood glucose, GE), evolution (death or re-

covery). Gestational age was estimated from the date of the last menstrual period and/or from ultrasound if performed before 12 weeks and/or from the Finnstrom morphological score [5]. Since the term is defined by gestational age, any birth between 28 and 36 weeks and six days was considered preterm and after 42 weeks as post-term [6]. Birth weight was analyzed from the Luchencho and Leroy curves to establish trophicity. Hypotrophy is defined as a weight below the tenth percentile, which is the second standard deviation [6].

The statistical analysis was done with SPSS software version 20.0. The comparison of the qualitative variables was carried out by the KHI 2 test and the Fischer test in case of insufficient numbers. A p value strictly less than 0.05 and an odds ratio (OR) whose 95% confidence interval (CI) did not exceed 1 were considered statistically significant.

3. Results

3.1 Flow Diagram

During our study period, 2885 newborns were admitted to the neonatal block.

We analyzed 2080 dossiers.et used 250 files taking into account our inclusion and non-inclusion criteria. The prevalence of maternal haemoglobinopathy was 08.6% (**Figure 1**).

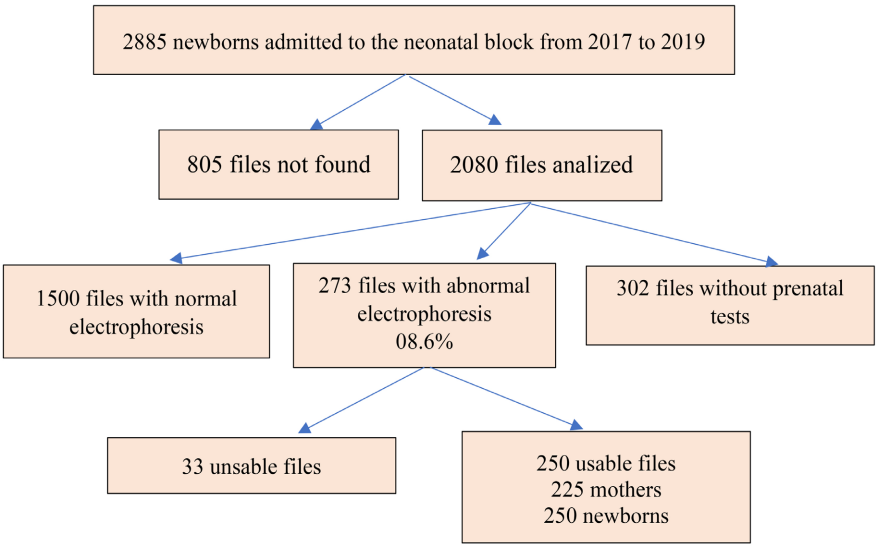

Figure 1. Prevalence of maternal haemoglobinopathy.

3.2. Characteristics of Mothers

The average age of mothers was 28.99 years and the most represented age group was between 18 and 35 years old (70.2%). The mothers were of Ivorian nationality (68.8%), resided in Abidjan (95.5%) and 42.6% of them were unemployed. There was a notion of spontaneous abortion in 22% of cases and a history of stillbirth in 3.5% of cases. Twenty-five mothers were carriers of twin pregnancies. The mean height was 2.8 and the mean parity was 1.32. The prenatal work-up was incom-

plete in 64.4% of cases and a haemoglobin level of less than 11 g/dl was noted in 44.8% of the mothers. They had major sickle cell disease in 16% of cases. Among the major forms, the double heterozygous SC form was the most common (47.22%), followed by the homozygous SS form (19.4%) and the forms associated with thalassemia (33.4%). The sickle cell trait AS was present in 37.7% of cases and hemoglobinosis C appeared only in the heterozygous AC form (36.8%). Complications encountered during pregnancy were eclampsia (7.1%), anaemia (2.6%) and retroplacental hematoma (1.1%). Table 1 summarizes the characteristics of the mothers and the electrophoretic profile of the mothers is presented in Table 2.

Table 1. Characteristics of mothers.

Variables	Number N = 225	Percentage %
Age (year)		
<18	10	4.4
[18 - 35]	158	70.2
≥35	57	25.3
Nationality		
Ivoirian	155	68.8
Non Ivoirian	70	31.2
Place of residence		
Abidjan	215	95.5
Interior and suburbs	10	4.5
Profession		
No profession	111	49.3
Student	32	14.2
Informal sector	76	33.7
Employed	31	13.7
Number of pregnancies		
1	65	28.8
[2 - 4]	90	40
>4	70	31.2
Number of births		
0	89	39.6
1	56	24.8
[2 - 4]	65	28.8
>4	15	6.6

Continued

Maternal history		
Miscarriage	50	22
Intrauterine fetal death	8	3.5
Pregnancy monitoring		
Prenatal consultation ≥ 4	189	84
Incomplete prenatal	145	64.4
Check-u		
Complications during pregnancy		
Eclampsia and high blood pressure	16	7.1
retroplacental hematoma	6	2.6
Vaso-oclusives crises	11	4.8
Severe anemia	7	1.1
Type of pregnancy		
Single	200	88.8
Gemmellar	25	11.2

Table 2. Distribution of dams by hemoglobin phenotype.

Hemoglobin phenotype		Number	Percentage (%)
Major forms n = 36 (16%)	SC	17	47.2
	SAFA2	8	22.2
	SS	7	19.4
	SFA2	4	11.2
Minor forms n = 189 (84%)	AS	85	45.0
	AC	83	44.0
	ASA2	18	9.5
	AFC	3	1.5

3.3. Characteristics of Newborns

Most of the newborns (78%) had been referred by the maternity ward of the Cocody University Hospital, within the first six hours of life for 59.6% of them. There was a predominance of women (sex ratio = 0.87). Almost half of newborns were born by caesarean section (44%) and 23.2% of newborns were preterm infants. In 74.14% of cases, these were medium prematurity (28 - 32 weeks + 6 days). The mean birth weight was 2778 g with extremes of 600 g to 4950 g. In 29.2% of cases,

the newborns were hypotrophic. This hypotrophy was most often harmonious (89%). An Apgar score of 7 or less at the 5th minute was found in 36.8% of cases.

The reasons for admission were, in order of frequency, prematurity (23.2%), an Apgar less than 6 (21.6%) and suspicion of maternal-fetal infection (14%).

Physical examination of the newborns mainly revealed neurological signs (41.6%), respiratory distress (33.6%) and pallor 26.7%. On the complete blood count, 30.8% of the newborns had normochromic normocytic anemia. Hyperleukocytosis was noted in 7.2% of cases and leukopenia in 16% of cases. C-Reactive Protein was positive in 36.8% of newborns and Thick Gout positive in 7.6% of cases. Hyperbilirubinemia greater than 10% of the body weight was present in 4.4% of them. Table 3 presents the characteristics of newborns and Figure 2 shows the main diagnostics.

Table 3. Characteristics of newborns.

Variables	Number (N = 250)	Percentage %
Route of delivery		
Low lane	140	56
Caesarean section	110	44
Age at entry (hours)		
<6	149	59.6
>6	101	40.4
Sex		
Male	116	46.4
Female	134	53.6
Birth weight (grams)		
<2500	82	33
>2500	168	67
Term		
Prematurity	58	23.2
Term	191	76.8
Trophicity		
Hypotrophic	73	29.2
Normotrophic	151	60.4
Macrosomal	26	10.4
Apgar at 5 minutes		
<7	92	36.8
>7	158	63.2

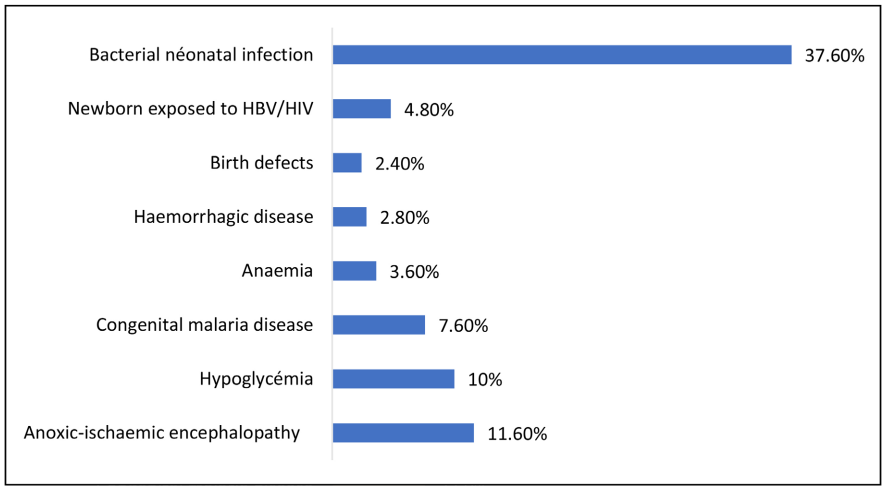

Figure 2. Distribution of newborns according to frequency of selected diagnoses.

3.4. Study of Mortality

The mortality rate among newborns admitted to hospital was 14.8% and the majority of deaths occurred during the first week of life (94.5%). The main causes of death are listed in Table 4.

Table 4. Leading causes of death.

Causes of death	Number N = 37	Percentage
Neonatal bacterial infection	6	16
AIE	13	35
Hypoglycaema	2	6
Anaemia	3	8
Prematurity	9	24
Birth defects	4	11

AIE = Anoxic-ischaemic encephalopathy.

3.5. Profile of Newborns Born to Mothers with Major Sickle Cell Syndromes

Mothers with major sickle-cell syndrome were twice as likely to give birth to a low-birth-weight infant. The difference observed was statistically significant (p = 0.046, OR = 2.05). In 53% of cases, major hemoglobinopathic mothers had a hypotrophic newborn, compared with 25% of minor hemoglobinopathic mothers. Regarding morbidity, newborns of mothers with a major form of sickle cell disease had twice the risk of contracting a neonatal bacterial infection (p = 0.009, OR = 1.82). However, neonatal mortality was not statistically associated with the mother's electrophoretic profile (p = 0.09) (Table 5).

Table 5. Profile of newborns of mothers with major sickle cell syndromes.

Characteristics of newborns	Maternal haemoglobin phenotype		P
	Major forms	Minor forms	OR
	n = 36	n = 214	CI
Delivery method			
Vaginal delivery	14 (39%)	97 (45%)	0.47
Caesarean section	22 (61%)	117 (55%)	0.77
			[0.37 - 1.59]
Gestational age (weeks)			
<37	8 (22%)	50 (23%)	0.88
≥37	28 (78%)	164 (77%)	0.94
			[0.4 - 2.19]
Birth weight (grams)			
< 2500	17 (47%)	65 (31%)	0.046
≥ 2500	19 (53%)	149 (69%)	2.05
			[1.01 - 4.1]
Trophicity			
Hypotrophic	19 (53%)	54 (25%)	0.08
Non hypotrophic	17 (47%)	160 (75%)	0.53
			[0.26 - 1.08]
Apgar at 5th minutes			
<7	14 (39%)	78 (36%)	0.77
≥7	22 (61%)	136 (64%)	1.14
			[0.54 - 2.29]
Neonatal bacterial infection			
Yes	18 (50%)	76 (36%)	0.009
No	18 (50%)	138 (64%)	1.82
			[0.89 - 3.7]
Hypoglycaemia			
Yes	6 (17%)	19 (9%)	0.149
No	30 (83%)	195 (81%)	2.05
			[0.76 - 5.65]

Continued

Anemia			
Yes	1 (3%)	8 (4%)	0.774
No	35 (97%)	206 (86%)	0.74
			[0.09 - 6.1]
Congenital malaria disease			
Yes	1 (3%)	11 (5%)	0.539
No	35 (97%)	203 (95%)	0.53
			[0.07 - 4.24]
Mortality			
Deceased	2 (6%)	35 (16%)	0.09
Living	34 (94%)	179 (84%)	0.34
			[0.07 - 1.31]

4. Discussion

Our findings are limited by the retrospective nature of our study. The files were not sufficiently detailed, particularly concerning follow-up of sickle cell disease during pregnancy, and several of them could not be examined because they were missing from our archives. On the other hand, in the context of our practice, bacterial infection of the newborn is rarely documented, given the high cost of bacteriological investigations. The majority of women were unemployed (42.6%) or worked in the informal sector (29.3%) and the prenatal work-up, which remains the responsibility of the patients, was incomplete in 64.4% of cases. The diagnosis of neonatal bacterial infection is most often based on anamnestic data, the newborn clinical condition, biological results and the positive outcome of antibiotic treatment.

The electrophoretic profile was comparable to that found by some African authors [7] [8]. Among the major forms of hemoglobinosis, the double heterozygous SC form was the most common (47.22%), followed by the homozygous SS form (19.4%) and the forms associated with thalassemia (33.4%).

Pregnancy in a mother who is a carrier of major forms of hemoglobinosis in general and sickle cell disease in particular is at high risk for the mother, the fetus and the newborn. Pregnancy worsens the medical complications of the disease, and the disease complicates pregnancy, leading to high maternal and perinatal mortality [9]. The usual complications in the mother and the fetus are vaso-occlusive crises, anaemia, infection, placental vascular complications (pre-eclampsia, retroplacental hematoma, growth retardation in utero and fetal death in utero), prematurity [10]. Several studies in the literature show that these complications

can also occur in patients with heterozygous forms of AS or AC during pregnancy [11] [12]. In our series, mothers had a history of stillbirth in 3% of cases. Eclampsia (14.4%), severe anaemia (6.3%), HRP (5.4%), vaso-oclusive crisis (4.8%) were the main complications found during pregnancy. Nearly a quarter (22%) of newborns born to mothers who were carriers of major forms were preterm infants. Low birth weight and hypotrophy were found in 47% and 53% of cases respectively. Newborns of mothers with major hemoglobinopathy were twice as likely to have low birth weight in our study ($p = 0.046$, OR = 2.05 CI [1.01 - 4.1]). These neonatal adverses have also been found by other authors [13]-[15].

In addition, mothers with major hemoglobinopathic diseases were more likely to have newborns with neonatal bacterial infection ($p = 0.009$, OR = 1.82 CI [0.89 - 3.7]). This high rate of neonatal infection seems to be overstated without bacteriological evidence. However, the frequent occurrence of infectious diseases in pregnant sickle-cell patients, especially in the third trimester of pregnancy, could explain this fact. Moreover, neonatal infection is the leading cause of hospitalization in our unit [7].

The mortality rate of 14.8% was comparable to those found in other studies [15]. The main etiologies of death in the two groups of newborns were: anoxoischemic encephalopathy (35%), prematurity (24%), neonatal bacterial infection (16%) and anemia (8%). Our results were consistent with those in the literature [16].

Newborns should be tested for hemoglobinopathies as soon as possible. Systematic screening has proved highly effective in reducing infant mortality, as well as severe infectious, anemic and neurovascular complications in early childhood [17] [18].

For early care of children born to mothers with hemoglobinopathies, we need to extend neonatal screening to the various peripheral health facilities, and build the capacity of health-care personnel.

5. Conclusion

Pregnancy with a hemoglobinopathic mother is at high risk for both the fetus and the newborn. Low birth weight, hypotrophy, prematurity, infection, were more common in newborns born to mothers with a major form of sickle cell disease. Mortality was high for both groups and the leading causes of death were preterm birth and IAE. In view of this high morbidity and mortality, a well-codified care of newborns of hemoglobinopathic mothers is essential from birth, starting with the generalization of the systematic newborn screening program for hemoglobinopathies in the various health centers. A study is needed to better understand the prevalence of these newborns and identify possible risk factors for morbidity and mortality.

Conflicts of Interest

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

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