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Epidemiological and clinical profile of alloimmunized children with sickle cell disease hospitalized in four hospital departments in Libreville

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Abstract

Sickle cell disease is a hereditary disease of the hemoglobin that provides blood transfusion and is responsible for the occurrence of alloimmunization in children with sickle cell disease.

Objective: The main objective is to describe the epidemiological and clinical profile of alloimmunized children with sickle cell disease hospitalized in four hospital departments in Libreville.

Materials and methods: This was a prospective descriptive, analytical study that took place over a period of seven months. We included all children with sickle cell disease, whether or not they were being monitored and hospitalized for acute anemia with a history of blood transfusion.

Results: During our study period, we included 71 children with sickle cell disease. The average age of the children was 80.2±55.4 months. The medical follow-up of children with sickle cell disease was correct 38% (n=27). The inter-critical hemoglobin level was 7g/dl. The medical history was found on average 3 blood transfusions of packed red blood cells. The blood group O positive was the most common 49.3% (n=). Packed red blood cells were the only labile blood product transfused 100% (n=71). The post-transfusion gain in hemoglobin was 1.48±1.3g/dl. The phenotype when incompatible was linked to a low post-transfusion gain. Splenomegaly and jaundice were the post-transfusion complications found with respectively 62% (n=44) and 36.6% (n=26). The Coombs test was positive 26.8% (n=19).

Conclusion: The phenomenon of alloimmunization remains unknown and underdiagnosed in children with sickle cell disease. The presence of clinical signs of post-transfusion hemolysis requires specific tests to be performed.

Keywords: Sickle cell disease; Transfusion; Alloimmunization; Gabon

1. Introduction

Sickle cell disease is the most widespread disease in Africa and in the world. In Gabon, it affects approximately 1.8% of the population with nearly 800 births of homozygous sickle cell children each year, representing a global prevalence of 5% [1, WHO2006]. It is a source of multiple complications, including acute hematological complications in children with sickle cell disease, malaria, and HIV infection [2]. Alloimmunization is an immune response resulting from the in vivo formation of irregular antibodies following the introduction of blood group antigens from individuals of the same

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species with an onset time of 3 to 21 days after transfusion. This is a little-known phenomenon. In order to contribute to strengthening the immunological safety of transfusion, we proposed to conduct a preliminary study on alloimmunization in children hospitalized in four hospitals in our capital. The main objective is to describe the epidemiological and clinical profile of alloimmunized children with sickle cell disease hospitalized in four hospital departments in Libreville. This is a prospective, descriptive, analytical and cross-sectional study, which took place in four health facilities (Libreville University Hospital (CHUL), Melen Estuary Regional Hospital (CHREM), Jeanne Ebori Foundation Mother-Child University Hospital, OMAR BO NGO ONDIMBA Army Training Hospital) over a period of 7 months. We included all hospitalized sickle cell children aged 6 months to 17 years, followed by sickle cell disease. Data collection was done on a standardized form. We studied the sociodemographic parameters of the children (age, sex) , history (follow-up, age of first transfusion, number of transfusions received, date of last transfusion; baseline hemoglobin level), clinical parameters (splenomegaly, jaundice) and biological parameters (NFS , Coombs test, RAI). The data were collected and entered into the Epi Info 7.2.2 software. Statistical analysis of the data was done by MS Excel software / Pvalue line . The significance threshold was set at *p<0.05.*

2. Results

During our study period , only 71 children with sickle cell disease were included. The mean age of the children was 80.2±55.4 months with a sex ratio of 0.87. The medical follow-up of the children with sickle cell disease was correct 38% (n=27). The inter-critical hemoglobin level was 7g/dl [5-9]. The medical history found an average of 3 blood transfusions of packed red blood cells. The blood group of the children was O positive in 49.3% (n=). Packed red blood cells were the only labile blood product transfused 100% (n=71). The post-transfusion gain in hemoglobin was 1.48±1.3g/dl. The phenotype when incompatible was linked to a low post-transfusion gain. Splenomegaly and jaundice were the post-transfusion complications found with respectively 62% (n=44) , 95% CI [49.7; 73.2] and 36.6% (n=26), 95% CI [25.5; 49.7] . The Coombs test was positive 26.8% (n=19) , 95% CI [16.9; 36.8]) .

Table 1 Summarizes the biological characteristics before transfusion

	mean (standard deviation)	**median [Q25-75]**	**min**	**max**
Age of first transfusion (in months)	17.8 (14.7)	12.0 [8.00; 24.0]	4.00	84.0
Hematocrit	11.7 (4.24)	19.0 [16.0; 22.0]	7.40	26.2
Hemoglobin input (g/dL)	5.1 (1.8)	5.00 [4.00; 6.30]	1.80	7
Gain in Hemoglobin	1.48 (2.12)	1.30 [0; 3]	-7.00	5.50
Number of transfusions	2.8 (1.3)	4 [2;6]	1	13
Volume of blood transfused	260 (101)	250 [178;321]	90	460

There is a correlation between the number of transfusions received and the inter-critical hemoglobin level. Figure 1 shows that the more the subject has been transfused, the lower his baseline level is with a correlation coefficient of -0.234 CI 95 (-0.413; -0.0370) p =0.021 (Figure 1)

We did not find any significant association between hemoglobin gain and blood group, number of previous transfusions and gender (Table 2)

Table 2 Relationship between alloimmunization and other factors

	Coombs test NEGATIVE (n = 52)	**Coombs test (n = 19)**	***p***
Age (median)	70.5 [36.0; 111]	72.0 [35.0; 95.5]	0.88
Age of first transfusion (median)	12.0 [8.00; 16.5]	15.0 [7.50; 36.0]	0.39
Hematocrit (median)	0.190 [0.170; 0.211]	0.18 [0.115; 0.245]	0.42
Hemoglobin at entry (median)	5.00 [4.00; 6.22[	4.90 [3.90; 6.30]	0.62
GSRH n (%)			
O+	26 (50%)	9 (47%)	0.96
A+	13 (25%)	4 (21%)	-
B+	11 (21%)	5 (26%)	-
AB+	2 (4%)	1 (4%)	-
Number of transfusions received n (%)			
	11 (21%)	5 (26%)	0.89
	12 (23%)	3 (16%)	-
	2 (3.8%)	1 (5.3%)	-
	27 (52%)	10 (53%)	-
Phenotype n (%)			
Compatible	51 (98%)	1 (5.3%)	<0.001
Incompatible	1 (1.9%)	18 (94.3%)	-

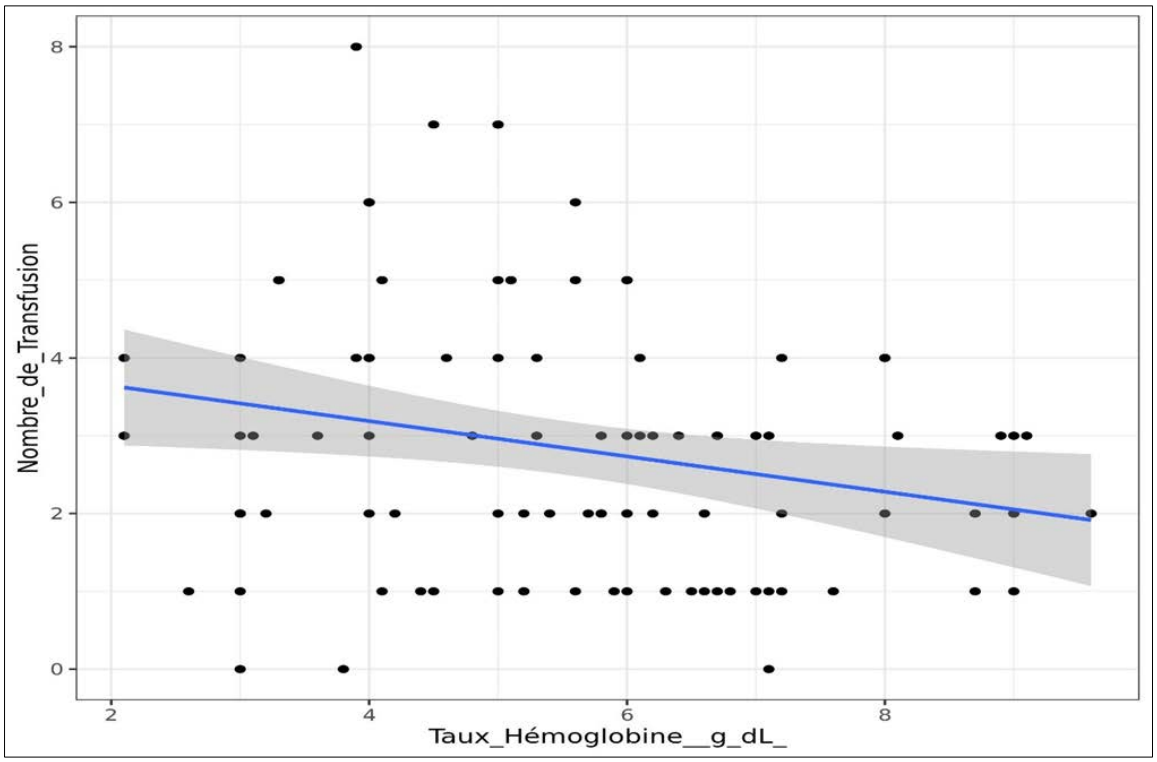

Figure 1 Relationship between the number of transfusions and the inter-critical rate of haemoglobin

3. Discussion

Sickle cell disease is a public health problem in Gabon. The majority of people with this disease live in Black Africa with prevalences varying between 10 and 20%. During this study, we were faced with some limitations such as hemolyzed samples, limited reagent stocks, reduced activity in some services following the Covid 19 pandemic and finally the lack of identification of the different antibodies due to a lack of funding. Despite all these shortcomings, the quality of our work was not affected.

We found a female predominance with a sex ratio of 0.8. This result is similar to that found by Mimbila et *al.* 0.95 [dr mimbila]. This result corroborates the data in the literature which states that the female sex would immunize twice as quickly as the male sex [6,11]. The average age of our patients was 6 years. Our result is similar to that of Macouba et *al* and that of the study carried out in Senegal [5] . In Gabon, early diagnosis of sickle cell disease is rarely made before the age of 2 years and neonatal screening is not systematic. Furthermore, we were unable to establish a link between age, sex and the occurrence of alloimmunization as described by some authors [11]. The explanation certainly lies in the size of our sample.

Most of our children with sickle cell disease had regular monitoring. These results corroborate those of the team of Minto'o et *al* . Who found 72% of children with sickle cell disease correctly monitored against 29% [7]. Correct monitoring of children with sickle cell disease exposes them less to sickle cell syndrome and especially to the occurrence of hemato-immunological complications.

The majority had an O positive blood group, AB group was rare. The same observation was made by Malumba et *al* [8]. The sampling being random, this predominance may be related to the number of children enrolled or to the fact that it represents the majority blood group in the general population.

In several African countries, blood transfusion is performed only taking into account ABO and Rh compatibility without seeking the compatibility of other erythrocyte systems such as the Kell, Kidd, Duffy, Lewis and MNSs systems, the antigens of which are all equally immunogenic. Such a practice carries risks, particularly in subjects who are often transfused, such as children with sickle cell disease. Our study revealed that 26.8%, or approximately 1 in 4 children with sickle cell disease, were alloimmunized. Some studies had found approximate rates of 16% in Senegal and 4.4% in Mali [2,9]. The only statistically significant factor was the phenotype. Determination of the phenotype may be necessary

to highlight expression variants in the Rh system that may have an impact on the occurrence of alloimmunization. This very high result in our study is probably also linked to the lack of medical monitoring of these children. Children who presented with post-transfusion splenomegaly had a positive Coombs test. Some authors such as Mick Ya Pongombo Shongi et *al* in Kinshasa noted nearly 73.2% of persistent splenomegaly. This splenomegaly would be evidence of post-transfusion hemolysis.

In Africa, several studies have been conducted on the biological effectiveness of blood transfusion by measuring weight gain and/or hematocrit. In Gabon, this gain was 2.9g/dl, in Mali 4.86g/dl [2, 11]. The low weight gain in our study confirmed post-transfusion hemolysis.

4. Conclusion

Alloimmunization is little known and underestimated. It is present in transfused sickle cell children in Gabon. In our work, we were able to note several factors that may be associated with it, including phenotype, weight gain, sex and the presence of splenomegaly and/or jaundice after transfusion reflecting a hemolytic character.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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