



# Anti-Erythrocyte Allo-Immunization to Sickle Cell Disease Patients Followed in Transfusion Therapy Unit of the National Blood Transfusion Center of Abidjan Côte D'Ivoire

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**Abstract:** The objective of this study is to evaluate the frequency of post-transfusion anti-erythrocyte allo-immunization to sickle cell patients in order to propose strategies of optimal blood safety in Côte d'Ivoire. It is a prospective study (January to December 2013) of patients with major sickle cell disease enrolled in the transfusion therapy unit of the National Blood Transfusion Center (CNTS) in Abidjan. The red blood cells have been phenotyped and compatibilized by indirect Coombs test in the ABO and Rh Kel systems. The search for irregular antibodies was performed before each transfusion episode. The incidence of post-transfusion anti-erythrocyte allo-immunization to the sickle cell disease patients were high (12/42 or 28.6%). We identified 14 allo-antibodies essentially anti-Rh specificity (12/14) with a high prevalence of anti-E allo-antibodies (6/14) and anti-C (4/14). None anti-Kel antibodies was found. This study raises the risk of allo-immunization in non-phenotyped and non-compatibilized transfusions, especially in sickle cell multitransfused. The erythrocyte phenotyping should be systematic to all major sickle cell patients.

**Keywords:** Sickle Cell Anemia, Anti-Erythrocyte Alloimmunization, Transfusion

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## 1. Introduction

The management of sickle cell disease often requires the use of blood transfusion. It helps to prevent or treat some complications with a simple blood transfusion or exchange transfusion in an acute setting or during a transfusion protocol in the long term. Its effect is twofold since improves the oxygen-carrying capacity of the blood by raising the Hb and reduce the harmful effects of HbS by reducing its percentage in favor of HbA. Transfusion is not without risk to these patients. The major immunological risk of transfusion is the anti-erythrocyte alloimmunization which can lead to severe immune hemolytic accidents and

transfusion dead lock situations. The allo-immunization is a common occurrence to sickle cell disease patients receiving multiple transfusions about 4 to 40% [1]. Regular immunohematological monitoring is therefore necessary and is an indispensable part of the management of these multiple transfusions. This will create a file for each patient and to know, at anytime, the history of the results of its research irregular antibodies. The lack of knowledge of the history could lead to the attribution of pheno-incompatible red concentrates blood cells which will be at the origin of a hemolytic transfusion accident by reactivation of an immunological allo-antibody. It is reduced by phenotyped and compatibilized blood transfusion policies to these polytransfused patients [1]. However, the immunological risk

is increased in general when a transfusion is practiced in emergency, which is often the case in Côte d'Ivoire where the prevalence of carriers of HbS is 14% [2]. At the national blood transfusion center (NBTC) in Abidjan, polytransfused patients for hemoglobinopathies are regularly monitored. The aim of our study was to determine the frequency of anti-erythrocytic allo-immunization to sickle cell patients followed in the transfusion therapeutic unit (UTT) to the NBTC of Abidjan in Côte d'Ivoire in order to propose strategies for strengthening transfusion safety.

## 2. Patients and Methods

We conducted a prospective and descriptive study with systematic inclusion of major sickle cell patients transfused at least once in the transfusion therapy unit of NBTC in Abidjan Côte D'Ivoire from January to December 2013. The study sample consisted of 42 sickle cell patients. Were included in our study the major sickle cell disease (SS,SC,Sβ°) with a transfusion history. We have consistently achieved the ABO blood group and Rh Kel phenotype in all patients. Blood groups ABO, Rh1 were determined using the plate technique with anti-A, anti-B, anti-AB and anti-D test serum from the BIORAD laboratories. Rh Kel phenotypes were determined by gel filtration technique using DiaClon Rh-Subgroups cards + K (BIORAD, France).

Before and after each transfusion, we performed the search for irregular agglutinin. To do this, the technique of Coombs indirect-low ionic strength gel filtration (Diamed), including a panel of O red cells type produced at the center and containing the most important regulatory antigens in terms of transfusion safety was carried out.

Panels of three red blood cells for screening and 11 for identification were used.

The patients were transfused with red blood cells compatible in ABO-Rh and Kel.

Data analysis was performed using Epi Info Version 6.4d.

## 3. Results

**Table 1.** Distribution of patients by age, sex and hemoglobin phenotype.

Parameters	Number	Percentage
AGE GROUP (year)		
[0-15]	12	28,6
≥16	30	71,4
Age mean: 24,45; extrêmes: 4-68		
SEX		
male	21	50
Female	21	50
Sex-ratio1(50/50)		
HEMOGLOBIN PHENOTYPE		
SSFA2	32	76,2
SFA2	9	21,4
SC	1	2,4
SAFA2	0	0

The mean age of the patients was 24.45 years with extremes of 4 years and 68 years. Adults were the majority in 71.4% of the cases.

There were as many male subjects as female subjects (Sexratio=1).

The homozygous phenotype hemoglobin (SS) predominated in 76.2% of the cases.

**Table 2.** Patients distribution according the ABO blood group.

Blood Group ABO	Number	Percentage
A	9	21,4
B	8	19,1
AB	2	4,8
O	23	54,7
Total	42	100

Just over half of patients (54.7%) had blood group O

**Table 3.** Patients distribution according to the Rh phenotyp Rh Kell.

Phenotype Rh	Number(n=42)	Percentage
Dccee(D+C-E-c+e+)	23	54,7
DccEe(D+C-E+c+e+)	6	14,3
DCcee(D+C+E-c+e+)	6	14,3
DCEee(D+C+E+c+e+)	1	2,4
DccEE(D+C-E+c+e-)	1	2,4
ddCee(D-C+E-c+e+)	2	4,8
ddccee(D-C-E-c+e+)	3	7,1
Phenotype Kel	Number(n=42)	Percentage
Kel négatif	40	95,2
Kel positif	2	4,8

The phenotype Dccee was most frequently observed in the Rh system (54.7%) followed by phenotype DCcee (14.3%) and DccEe (14.3%).

The majority of patients had negative phenotyp Kell (95.2%).

Number of transfusions received.

**Table 4.** Patients Distribution according to the number of transfusions received.

Number of Transfusion	Number	Percentage
1	5	11,9
2-5	11	26,2
6-10	15	35,7
>10	11	26,2
TOTAL	42	100

1/3 patients (36.1%) received at least 4 transfusions.

**Table 5.** Patients distribution according to the presence of irregular antibodies.

RAI	Number	Percentage
Négative	30	71,4
Positive	12	28,6
Total	42	100

The search for irregular agglutinin was positive in 28.6% of cases.

**Table 6.** Patients distribution according to the specific irregular Ac.

Irregular Antibody*	Number(14)
anti-D	1
anti-C	4
anti-E	6
anti-c	-
anti-e	1
anti-K	-
anti-S	1
nonidentify	1

\*A patient may have more than one irregular antibodies: one patient with anti-D +anti-C, another with anti-E + anti-S.

All the antibodies identified (total14) were irregular immune mostly directed against antigens of the Rh system with a predominance of specificities anti-E and anti-C.

## 4. Discussion

The average age of the patients in transfusion program in the therapeutic unit of the NBTC of Côte d'Ivoire was 24.45 years (range: 4 years and 68years). Children (1-15 years) accounted for 28.6% and 71.4% adults. These results are superimposed on those of Diarra in Mali who observed an average age of 21 years (range: 1 to 62 years) and children accounted for 32%, adults 68%. [3].

In our study, there was no sex-related predominance (21 female patients and 21 male sex ratio=1). This observation differs from studies conducted by Dembélé in Côte d'Ivoire which reported a sex ratio of 1.02 in favor of the male and Diarra in Mali which observed a female predominance with a sex ratio of 0.73.

Our patients were predominantly sickle cell homozygous SS (76.2%). This would be related to the severity of the disease in this form with the occurrence of acute or chronic complications. Our results are similar to those obtained by Diarra in Mali who obtained 72.2% of sickle cell anemia [3]. It is these complications that justify the indication of transfusion to these patients.

The distribution of antigens blood group in the ABO and Rh systems is comparable with those of previous studies conducted in Côte d'Ivoire [4] and elsewhere in Africa [5]. Infact, in most African series, the O group (54.7%) and the positive Rh group (Rh D+: 88.1%) and the phenotype Rh Dcece (54.7%) are predominantly found. Menier and al. observed in a French study of an Afro-Antillean sickle cell cohort the same distribution of the ABO and RH blood groups (51% of O, 93 % of D+ of which 54% of Dcece) [6].

Regarding the Kell phenotype, the majority of our patients was kell negative (95.2%). These results corroborate those of Siransy and al. [7] and Sekongo and al. [8].

The frequency of positive RAI was 28.6% (12/42). These all immunizations were observed during the initial review of the first track in the UTT. These patients were previously monitored and transfused into other clinical services. This frequency of anti-erythrocytic alloimmunization is far superior to those published in Mali by Diarra in 2011, ie 4.4% [3] or in Côte d'Ivoire by Malèwe in 2005, ie 4% [9].

It is close to those reported by Ben Amor in Tunisia in 2009 or 25.9 % [10], or by Dembélé in Côte D'Ivoire in 2013 ie 26.1% [11]. In 2008, Akré and al [2] had found a strong immunization of their patients in the order of 62.8%. Their result was comparable to Alarif [12] in 1985 (64%) and Olulohungbe [13] in 2001(76%).

In our study, positive RAI were the most observed in patients with transfusions greater than 4.

Patients enrolled in the long-term transfusion program who were transfused only to the UTT where phenotyping in Rh Kel and had the Laboratory Compatibility Test (EDCL) systematically prior to transfusions, and have not developed anti-Erythrocyte allo-immunisation.

Most of our patients received an average of 9 transfusions with extremes of 1 and 22 transfusions. We could not establish the exact time of immunization of patients transfused outside the UTT. Akre and al. [2] reported in their study immunization from the 4<sup>th</sup> transfusion. Pinto and al, reported a risk of developing an anti-erythrocyte alloimmunization 16 times higher in patients who received more than ten blood transfusions. [14].

Regarding the specificity of allo-antibodies, 14 antibodies were detected in our patients including 2 cases of association of 2 alloantibodies, mostly directed against antigens of the Rh system (12 anti Rh against 1 anti-S 1 unidentified and no anti-KEL) with a high prevalence of anti-E, anti-C specificities. The anti-erythrocyte allo-immunization is a relatively rare complication from the systematic use of red blood cell concentrates Rh Kel phenotyped because the majority of antibody once encountered appear in these [6] systems. This was well illustrated in a Tunisian study of 84 cases of hemoglobinopathies in which Ben Amor and al showed that the alloantibodies were mainly of Rh phenotype when using standard red blood cells [2]. In this study the specificities were essentially anti-E. With the use of phenotyped red blood cells, the number of alloantibodies was reduced to 3 with anti-FY1 and anti-JK2 specificities. This shows the utility of systematic Rh phenotyping in any sickle cell anemia in reducing the risk of post-transfusional anti-erythrocytic allo-immunization. Allo-immunization can be expressed either by the acquisition of one or more allo-antibodies which will make later transfusions difficult or by an immediate or delayed haemolytic accident [15].

We observed in our study 1 case of RAI positive with post-transfusion haemolysis associated also with hemochromatosis. It maybe associated with auto-immunization which may increase the risk of hemolytic accidents.

## 5. Conclusion

Sickle cell disease is a hemoglobinopathy whose major treatment remains the transfusion of red blood cells. However, this treatment is not without risk. This study shows the high frequency of post-transfusional anti-erythrocytic allo-immunization in sickle cell anemia. The factors influencing anti-erythrocyte alloimmunization mainly

concern transfused blood products. This requires the implementation of a preventive transfusion strategy to ensure optimal transfusion safety; to know: -transfusion of compatible Rh/Kel red blood cells and, if possible, FY JK and MNS;

- Regular immunological monitoring of polytransfused patients by the search for irregular agglutinins and the direct Coombs test.
- patients Informing and health care personnel about transfusion practices during sickle cell anemia and the problems associated with this therapy: alloimmunization can lead to clinical complications to polytransfused patients, including post-transfusion haemolysis, Obstetric future of female subjects.

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