



## Research Article

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# Factors associated to hemochromatosis in people living with sickle cell disease at Douala General Hospital (DGH) and Douala Laquintinie Hospital (DLH)

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## Abstract

**Context:** Sickle cell disease (SCD) is an autosomal recessive hereditary genetic haemoglobinopathy caused by a point mutation at position 6 of the codon causing a substitution for glutamic acid for valine. It is characterised by vaso occlusive crises, susceptibility to infections, chronic anaemia that will require a timely blood transfusion or the putting in place of a transfusions program in the case acute complications. In the long run, these multiple transfusions will have as consequence an iron overload and above a certain level will have serious cardiac, endocrine and articular effects hence the need for early screening with the help of serum ferritin. The goal of this study was to seek the associated factors to hemochromatosis in people living with SCD frequenting two hospitals in the town of Douala. **Methods:** It's was a descriptive and analytical transverse study. It was done over a period of 6 months from October 15, 2015 to 20th of April 2016. Included in this study was every person living with SCD in his/her majority age, documented hospitalised or followed up at outpatient consultations at DGH and DLH. During this study period we excluded every person with SCD who did not give an informed consent and all who had benefited from a blood transfusion in the past three months before the study. The recorded parameters were age, gender, past medical history of the person and serum ferritin levels. Data analysis was done with the help of the software, Epi-info 7. **Results:** A total of 201 persons with SCD were recruited and tested. The frequency of hemochromatosis was 20.9%. Male gender was the most represented (54.76%) than the female gender (45.24%) with a sex-ratio of 1.2; 1. Hemochromatosis was noted in 85.7% of people with SCD having had a blood transfusion. The mean number of erythrocyte concentrates was 7.5. Associated factors found in this study were; blood transfusion ( $p= 0.018$ ;  $r=+ 0.18$ ), poor general status ( $p<0.0001$ ), hepatomegaly ( $p= 0.02$ ), splenomegaly ( $p= 0.001$ ), follow-up ( $p<0.0001$ ), rural residency ( $p=0.006$ ). **Conclusion:** Hemochromatosis is frequent. Male gender is more concerned and the mean age is 14 years. Associated factors are poor general status, blood transfusion, hepatomegaly, splenomegaly, hospitalisation, follow-up and area of residence. It is important to look for hemochromatosis in people with SCD having the above characteristics so as to prevent cardiac and hepatic complications.

**Keywords:** Sickle cell disease, Serum ferritin, Blood transfusion.

## INTRODUCTION

SCD also at times referred to as sickle cell anaemia is the most widely spread haemoglobinopathy in the world. Its prevalence in Cameroon is 22.7%. It's transmission is autosomal recessive and results from a point mutation at position 6 of the  $\beta$  globuline (GAG  $\rightarrow$  GTG) found on chromosome 11, causing the substitution of glutamic acid by Valine at position 6 of the A segment of the  $\beta$  chain (HbS:  $\alpha_2 \beta_2$  S6Val) [1, 2].

It is characterised by a major syndrome constituted of chronic anaemia, susceptibility to infections and vaso-occlusive crises [3]. In its homozygous form it is responsible for many complications and blood transfusion constitutes one of the major therapeutic means [4]. That is why more than 60% of patients homozygous SS have been transfused at least once before the age of 18 years [5]. In 5 to 10% of cases, the patients are placed under a monthly transfusion program on a long term [6]. Each erythrocyte concentrate provides about 200mg of iron at the end of 10 to 20 transfusions of erythrocyte concentrates an iron overload defined as hemochromatosis installs [7, 8]. The goal of this work was to evaluate iron overload in people with SCD and to seek its associated elements.

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## METHODOLOGY

This study was carried out on persons with SCD, homozygous, followed up at the 'Centre de prise en charge de la drépanocytose Emmanuel Bilong' at DLH and at DGH. All two hospitals are specialised in the management of people living with SCD at Douala (Cameroon).

Was included in the study 201 individuals with SCD, homozygous, known and found in the inter-critical phase and having not been transfused in the past three months.

After obtaining an informed consent and ethical Clearance from the ethical committee for all the participants, we sought their past medical history that is; number of transfusions received, regular iron supplementation and regular follow up. Physical examination helped to evaluate the general clinical status and to look for hepatomegaly and splenomegaly.

A venous tap was done for serum ferritin calculation by the turbidimetry/latex method.

Hemochromatosis was defined as elevated serum ferritin level greater than or equal to 1000 ng/ml, no matter the age range [9].

The following reference values we're considered [10]:

- From 6 months to 15 years : 15-100 ng/ml,
- Adult male: 30-300 ng/ml,
- Adult female : 20-200 ng/ml

Data analysis was done with Excel and SPSS softwares. Statistical analysis were done using the student t test, Anova test and Chi squared test. The correlation between variables was sought using the person coefficient. Statistical limit was set at  $p < 0.05$ .

## RESULTS

### Demographical data

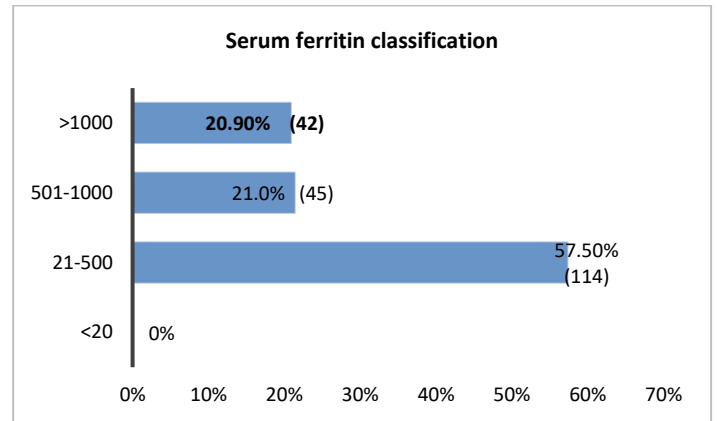
The study population had a total of 201 people homozygous and known SCD. The mean age was  $13.7 \pm 9.5$  years with extremes 61 years, and a sex-ratio MF of 1.03. The majority of people with SCD lived in an urban area that is 95.2%. The socio-demographic details are given in the table below.

**Table 1:** Socio-demographic classification of the population

	Proportion (%)	Number (n)
Gender: Male	49.25	102
Female	50.75	99
Residence: Rural	1.00	2
Urban	99.00	199
Educational level: None	7.00	14
Primary	44.00	88
Secondary	34.00	68
Tertiary	15.00	30

### Serum ferritin variation

Within the study population, 113 patients that is 56.20% had a normal serum ferritin level between 21 and 500 ng/ml. In 22.4% of cases (45), the serum ferritin level was high between 501 and 1000 ng/ml. In 20.9% of cases (42), the values were greater than 1000 ng/ml. We did not find any iron deficiency anaemia (serum ferritin < 20 ng/ml), as represented on figure 1.



**Figure 1:** Study population classification with respect to serum ferritin level groups

### Iron overload

Amongst the 42 patients who had a serum ferritin level greater than 1000 ng/ml, 19 (45.24%) were women and 23 (54.76%) were men. The mean ferritin level was  $1567.48 \pm 357.5$  µg/L with extremes of 1004 and 2150 µg/L. The mean number of blood transfusions received was 7 with extremes of 1 and >20. In our series, 142/201 of people with SCD HAD received at least once a blood transfusion. The mean serum ferritin level increased with the number of transfusions (Figure 2). We noted a positive correlation and a statistically significant difference ( $r = 0.14$  and  $p = 0.00$ ), between the number of pints of blood received and the serum ferritin level.

### Factors associated to hemochromatosis

Iron overload in this study was principally associated to clinical characteristics that is; poor general status ( $p = <0.0001$ ), hepatomegaly ( $p = 0.02$ ), splenomegaly ( $p = 0.001$ ) and blood transfusion ( $p = 0.01$ ).

## DISCUSSION

We carried out this study with the aim to determine the frequency of and the associated factors to hemochromatosis in people living with SCD in our context.

On a venous blood tap we carried out a serum ferritin determination. We considered as having hemochromatosis all those who had a serum ferritin >1000 ng/ml without taking into consideration the inflammatory laboratory exams and the cytolytic laboratory exams. Nevertheless we think these results are a reflection of the actual values in people living with SCD.

The confirmation diagnosis of iron overload in patients with SCD is based on the determination of the liver iron concentration [6,7]. Nevertheless this technique being invasive and not risk free the determination of serum iron level offers an alternative not only in the diagnosis but also in the follow up of those on chelating treatment [10]. Serum ferritin can be influenced by different factors like inflammation, infection and hepatic cytolysis [11]. The frequency of 20.9% of iron overload observed in this study is similar to that of Rondeau-Lutz in France where the frequency was 23% [12]. On the other hand, Tshiloloin Congo had 22% of cases of hemochromatosis taking as reference the serum ferritin < 500 ng/ml [9]. The study by Hafsia *et al* in Tunisia was done on ninety-five people with SCD and the frequency of hemochromatosis was 41.5% [5]. This author had considered a serum ferritin level greater than 300 ng/ml.

The difference in the prevalence between these different studies can be explained partly by the variations in the limits of serum ferritin considered.

In this study, the participants had received at least one blood transfusion in 85.7% of cases. Blood transfusion is a therapy frequently used in the management of the complications of SCD. It represents the principal factor associated to overload [9, 10]. Every erythrocyte concentrate brings in about 200mg of iron and the latter brought in by every transfusion accumulates in the organism and at the end of 10 to 20 blood transfusions, an overload appears [6-8].

The frequency of hemochromatosis increased with the number of erythrocyte concentrates received (>10). We agree with certain authors that between 10 and 20 erythrocyte concentrates, an iron overload appeared [6-8].

Many studies have shown an association between blood transfusion and hemochromatosis. Hafsia et al in Tunisia in 2011, Fung *et al* in 2007, as well as Davies et al in America in 1984 reported that serum ferritin increased in a significant manner as long as the patients were transfused [13-15]. Transfusion should therefore be a factor that plays a non-negligible role in the development of iron overload in people with SCD [14]. In this study, we noted that a person with SCD transfused has 2.5 times more risk to develop hemochromatosis.

For certain authors, there exists a good correlation between the number of blood pints transfused and the serum ferritin level. The values of the serum ferritin significantly increased in persons with SCD polytransfused compared to those who have never been transfused [9, 11, 14-16].

The correlation between the number of erythrocyte concentrates received and the serum ferritin in this study ( $r=+ 0.18$ ) was less strong than that found by Lina et al in 2008 ( $r=+ 0.40$ ) [17], Hafsia *et al* in 2011 ( $r=+0.74$ ) [13] and Porter et al in 1987 ( $r=+ 0.86$ ) [16].

These differences could be explained by the fact of the variation in the norms of the serum ferritin in the different study populations.

All the transfusions in our series were done by the simple method and generally with whole blood. Whereas this technique is the greatest provider of iron overload with respect to the other transfusions methods [5, 6]. Be it in the case of simple blood transfusions or exchange transfusions in the long run, the relationship between serum ferritin level and the transfusion load has been established, as well as in the present study, by other authors [5]. We found as clinical associated factors hepatomegaly and splenomegaly. In this study, the patients with SCD had respectively 3.4 and 3 times more risk of developing hemochromatosis. These results may be explained by the fact that the liver being and iron storage organ, in the case of overload, it will increase in size as well as the spleen due to the fact that there will be chronic haemolysis. Hepatomegaly and splenomegaly could equally mark either a hepatic cytolysis, an inflammatory syndrome or an infection which are generally the origin of a non-specific increase in serum ferritin during a blood test [16].

On the other hand we found out that the individuals with SCD follow up by a nurse and those living in a rural area had 4.8 times more risk of developing iron overload. This we explain in part by the lack of knowledge of the mechanism of action of haemolytic anaemia and the adequate follow up of SCD by the nursing personnel. On the other hand by the rarity of specialist hospital infrastructure in these areas, by the approximate management in the health centres present and high risk behaviours to develop this pathology (old practices of blood transfusion, iron supplementation and traditional remedies rich in iron).

## CONCLUSION

Iron overload is frequent in people with SCD followed up at Douala. The male gender is more concerned by this pathology. It is associated

with the number of blood transfusions received, to splenomegaly, to hepatomegaly and to poor general status.

## What is known about this subject?

Includes a maximum of 3 points on what is known about this subject:

- Blood transfusion is associated to the development of iron overload in the SCD patient.
- Iron overload is associated to an alteration in the clinical status of the patient, hepatomegaly and splenomegaly.

## What new thing does your study bring about?

- hemochromatosis is frequent in Douala-Cameroon: 20.9%
- Iron overload touches the male gender more and those less than 10 years.

## Conflict of interests

The authors declare no conflict of interest.

## Authors' contributions

All the authors contributed to the realisation of this piece of work. All the authors declare to have read and approved the final version of the manuscript.

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