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Factors Associated with Splenomegaly amongst Patients with Sickle Cell Disease in Cameroon

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Abstract

Introduction: Sickle cell disease is the most common hemoglobinopathy in the world. Sickle cells are quickly fixed and destroyed by the elements of the reticuloendothelial system mainly in the spleen. It leads to a palpable increase in the volume of the spleen called splenomegaly. Splenomegaly is the cause of multiple complications that are relatively frequent and potentially serious in sickle cell disease, such as splenic sequestration seizures, spleen rupture, hypersplenism and splenic abscesses. We aimed at determining the prevalence of splenomegaly and to study the associated factors in patients with sickle cell disease. **Materials and Methods:** This was an analytical cross-sectional study, conducted from 1 January to 30 April 2019, at the Mother and Child Center of the Chantal BIYA Foundation. Patients were grouped into two groups: patients with splenomegaly (PS1) and patients without splenomegaly (PS0). As soon as we obtained the informed consent of the parents, we examined the children and recorded socio-demographic data, disease history and follow-up, documented complications, and clinical findings; then we performed the Rapid Malaria Diagnostic Test. The statistical analyzes were carried out using SPSS20 (Statistical Package for Social Sciences) and Microsoft Excel 2010 software. **Results:** We examined 403 children with sickle cell disease and 142 had splenomegaly (35%). Almost all of the study populations were homozygous SS. The Hackett 2 stage of splenomegaly was the most frequent (56.7%).

The most common physical sign among PS1 was the presence of abdominal scarring (50.7% vs. 19.4%). PS1 had significantly lower levels of Hb (6.94 ± 1.67 vs 7.62 ± 1.43 p = 0.003) and platelets (297.45 ± 146.25 vs 398.70 ± 163.73 p < 0.001) than patients without splenomegaly (PS0). However, the percentages of HbF (21.78 ± 10.48 vs 15.66 ± 9.20 p < 0.001) and malaria infection (74.6% vs 17.2% p < 0.001) were statistically higher among PS0. Logistic regression analysis determined that the factors associated with splenomegaly were: malaria, high fetal hemoglobin, low hemoglobin S, hepatomegaly, thrombocytopenia and use of non-steroidal anti-inflammatory drugs. **Conclusion:** Splenomegaly is a frequent physical sign of sickle cell disease in children and factors associated are malaria, high hemoglobin F, low hemoglobin S, hepatomegaly, thrombocytopenia and NSAID use.

Keywords

Sickle Cell Disease, Splenomegaly, Thalassemia, Malaria, Associated Factors

1. Introduction

Sickle cell disease is the most common hemoglobinopathy in the world [1]. Sickle cell disease is a hemoglobinopathy, secondary to the presence of abnormal hemoglobin (Hb), in the red blood cells, called Hb S. It is due to the replacement of glutamic acid by valine in position 6 on the beta chain of the globin protein [2]. The most widespread hereditary hemopathy in sub-Saharan Africa, it constitutes, according to the World Health Organization (WHO), a major public health problem [3] [4]. The prevalence of sickle cell trait (SA) in Central Africa is estimated at 25% [5]. In Cameroon, in 2016, Sack *et al.* found a prevalence of hemoglobin S at 18.2% in 703 newborns at Yaounde central hospital [6]. These HbS molecules, in a deoxygenated medium, have the property of polymerizing, thus deforming the red blood cells (RBCs) in the form of rigid sickles. Complications of sickle cell disease concern all organs, such as the spleen, which is affected early in the course of the disease [7]. In the medium term, progressive atrophy following multiple vaso-occlusive crises and infarction leads to splenectomy, the time to onset of which differs according to the authors; occurring in homozygous SS sickle cell sufferers at six years of age for some [8], while others find an increase in volume during the first decade of life [7]. In Africa, the prevalence of splenomegaly during sickle cell disease has been evaluated in Senegal at 17.5% [9]. This splenomegaly is more frequent during sickle cell disease with significant differences found between SC composite heterozygotes (32.3%) and SS homozygotes (16.5%) [8]. *Plasmodium falciparum* infection and the haplotype would play a major role in the persistence of splenomegaly in sickle cell patients from sub-Saharan Africa compared to African-American populations [9]. Splenomegaly gives rise to multiple relatively frequent and potentially serious complications in sickle cell disease, such as splenic sequestration crises, rupture of the spleen, hyper-

splenism and splenic abscesses. Therefore, we wanted to determine the prevalence of splenomegaly and to study the associated factors in subjects suffering from sickle cell disease.

2. Methods

2.1. Population, Location and Duration of Study

Our source population consisted of subjects with sickle cell disease regularly followed up at the Mother and Child Center of the Chantal BIYA Foundation (CME/FCB). This center has a sickle cell care unit which includes five doctors, assisted by a team of seven nurses and a psychologist, all of whom are committed to putting their know-how at the service of patients. It has a capacity of twelve beds spread over four rooms for an average of 600 hospitalizations, 2000 outpatient consultations for sickle cell patients per year, in addition to preventive and awareness-raising activities. This service also oversees the association of parents of children with sickle cell disease at the said hospital, which has more than three hundred members. The sectors concerned by our study were: the sickle cell care unit, the emergency department, the outpatient clinics, the meetings of the association of parents and children with sickle cell disease. We recruited patients over a 4-month period from January 1 ^{to} April 30, 2019

2.2. Selection Criteria and Sampling

We included in our study all patients: suffering from sickle cell disease, aged from six months to 15 years, having a hemoglobin electrophoresis less than 6 months old, regularly followed up. Was considered as a patient regularly followed-up: any patient having respected the control appointments, from the previous year until the moment of recruitment. All subjects who underwent a splenectomy, those who only had an electrophoresis made after blood transfusion less than 4 months ago, and those who did not sign the informed consent form were excluded from the study. We conducted an analytical cross-sectional study with both prospective and retrospective data collection. We conducted non-probability, consecutive, and non-exhaustive sampling. The minimum size of our sample was therefore 90 subjects according to a study carried out in Gabon which found a prevalence of splenomegaly at 37% in children with sickle cell disease [10].

2.3. Data Collection Procedure and Tools

Armed with our technical data sheet, we introduced ourselves to the parents of children, explained to them the study that we were conducting and invited them to authorize their child(ren) to take part. Once the informed consent form had been read and signed, we proceeded to the clinical examination of the child with sickle cell disease, under the benevolent presence of the parent. We consulted the medical files of the patients in search of additional information. When necessary, we made appointments and made phone calls to patients' parents. The palpation technique in search of a possible splenomegaly

was as follows: the patient being in the supine position, hips flexed, we placed one hand flat by slightly depressing the wall at the level of the left iliac fossa and by having the patient breathe in. We went up with each inspiration until the edge of the hand slipped under the ribs. We started very low in the left iliac fossa to screen for large splenomegaly. All our data was collected using pre-tested data sheets.

2.4. Data Management and Analytics

The data was recorded on anonymous collection sheets (to ensure the confidentiality of the results). The data was entered into a CS Pro 6.3 (Census and Survey Processing System) input mask. Statistical analyzes were carried out with SPSS20 (Statistical Package for Social Sciences) and Microsoft Excel 2010 software. The completed questionnaires were well checked before the data was entered manually by us, in the machine. A second check was done by an independent individual to avoid any error. The results were presented as tables, figures and expressed as a percentage or in numbers.

2.5. Ethical Considerations

Before starting the recruitment we obtained the validation of the scientific committee of the Higher Institute of Medical Technology, then an ethical clearance of the Institutional Ethics Committee of Research for Human Health of the University of Douala (CEI-UD). Subsequently, we obtained research authorization from the director of the CME/FCB.

3. Results

At the end of our recruitment, we conducted our study on 201 children with sickle cell disease, among whom 67 were carriers of splenomegaly (PS1) and 134 not carriers of splenomegaly (PS0).

3.1. Socio-Demographic Characteristics of the Study Population

Of the 403 subjects with sickle cell disease, aged 6 months to 15 years; 142 were carriers of splenomegaly, *i.e.* a prevalence of 35.2% (142/403). The PS0 were mostly between 6 and 10 years old (40.3%) with an average of 7.74 years. The female sex predominated in our sample (more marked among the PS1). This is shown in Table 1.

3.2. Clinico-Biological Profile of the study Population

Jaundice was statistically more common in PS0 than in PS1 (41.8% vs 26.9% p = 0.032). Concerning the physical signs, the most frequent was the presence of abdominal scarification scars more marked in PS0 than in PS1 with a significant difference; then come abdominal distension and hepatomegaly, which are statistically more frequent in PS1. The most represented stage in our study was Hackett stage 2 (56.7%).

Table 1. Demographic and clinical data of patients in the study.

	PS1 (%)	PS0 (%)	Total (%)
DEMOGRAPHIC CHARACTERISTICS			
Age			
6 months - 6 years	23 (34.3)	48 (35.8)	71 (35.32)
6 - 10 years old	27 (40.3)	43 (32.1)	70 (34.82)
10 - 16 years old	17 (25.4)	43 (32.1)	60 (29.85)
Sex			
Male	32 (47.8)	59 (44.0)	91 (45.3)
Feminine	35 (52.2)	75 (56.0)	110 (54.7)
CLINICAL CHARACTERISTICS			
Jaundice	18 (26.9)	56 (41.8)	74 (36.8)
Abdominal distention	26 (38.8)	4 (3)	30 (14.9)
Scarifications	34 (50.7)	26 (19.4)	60 (29.9)
Hepatomegaly	16 (23.9)	7 (5.2)	23 (11.4)
Pallor	49 (73.1)	112 (83.6)	161 (80.1)

PS1: Patient with splenomegaly; PS0: Patient without splenomegaly.

The most frequent circumstance of initial diagnosis of sickle cell disease was the vaso-occlusive crisis type of hand-foot syndrome in the two groups of individuals *i.e.* carriers and non-carriers of splenomegaly (40.3% and 56.7%), followed by severe anemia (26.9% and 17.2%). We consulted the vaccination record of each patient and recorded their vaccination status according to their age. The majority of patients did not have their vaccines up to date, regardless of their group.

In our sample, 33 PS1 have already been hospitalized or 49.25% against 78 PS0 or 58.21%. There was no significant difference between the two groups in terms of mean consultations/year. PS0 are generally more prone to hospitalizations than PS1. The mean number of hospitalizations/year, which was 1.97 ± 1.92 in PS1, was statistically lower than that of PS0, which is 2.39 ± 1.43. Among PS1, the most common reasons for hospitalization were severe anemia (51.52%). Vaso-occlusive crises (48.48%) came second, followed by infections (39.39%). However, the second group was more frequently admitted to hospital, in 52.56% of cases for vaso-occlusive crises, in 41.03% of cases for infections and in 38.46% of cases for severe anemia. The frequency of transfusions did not vary significantly between the two groups. There were no great differences in the frequency of occurrence of the various complications between the two groups.

Overall, PS0 were more medicated than PS1. The difference was significant for taking NSAIDs and folic acid. The hemoglobin electrophoresis profile of almost all of the individuals was of the SS type. Of 201 patients included, 199 were SS

homozygotes (99%), and 2 composite SC heterozygotes (1%). The frequencies of splenomegaly according to patient hemoglobin electrophoresis were: SS homozygotes: 32, 7%; SC composite heterozygotes: 100%;

The hemoglobin F level was on average equal to 21.78 ± 10.48 in PS1 and 15.66 ± 9.20 in PS0. This hemoglobin F level was statistically higher in PS1 than in PS0. In six patients, the presence of HbA was noted, apart from any context of recent transfusions. HbA had a similar level in PS1 and PS0.

Average hemoglobin and platelet counts were statistically higher in PS0 than in PS1. On the other hand, there were no significant differences in the mean number of white blood cells and reticulocytes between the two groups.

The vast majority of subjects in both groups of individuals slept under impregnated mosquito nets. We conducted a rapid diagnostic test for malaria to all our patients. The results obtained showed that the malaria infection was present in 74.6% of PS1 while only 17.2% of PS0 suffer from it. The mean frequency of blood transfusion since diagnosis was 2.261 (±2.781) in PS0 and 2567 (±2.781) in PS1, p = 0.506. The mean haemoglobin level on admission was lower in PS1 (6.96 ± 1.67) than in PS1 (7.62 ± 1.43), p = 0.003 as shown in Table 2.

3.3. Factors Associated with Splenomegaly

The factors associated with splenomegaly are: malaria, hepatomegaly, number of platelets, taking nonsteroidal anti-inflammatory drugs, fraction of hemoglobin F and fraction of hemoglobin S. Indeed, malaria is 15.26 times, hepatomegaly is 6.06 times, hemoglobin F fraction above 10% and platelets below 400,000 is more likely to be found in patients with PS. This is shown in Table 3.

4. Discussion

The main objective of our study was to determine the prevalence of splenomegaly and to study the associated factors in subjects suffering from sickle cell disease at the Mother and Child Center of the Chantal BIYA Foundation.

The overall frequency of splenomegaly in our patients was 35.2%. This result is similar to the 37.4% found by Thuilliez *et al.* in Gabon [11]. This prevalence is low, compared to that of 100%, reported in Yaoundé in 2018 by Nama *et al.* [12]. This difference could be due to a selection bias, splenomegaly being a constant criterion of acute splenic sequestration and this was the study population in the study by Nama *et al.* In West Africa, Ranque *et al.* in 2007, two series of Nigerian

Table 2. Relationship between frequency of transfusion and haemoglobin level in the sample population.

Factors	PS0 (SD)	PS1 (SD)	P-value
Mean number of transfusions since Sickle Cell Disease diagnosis	2.261 (± 2.781)	2.567 (± 2.781)	0.506
Mean Haemoglobin level on admission (g/dL)	7.62 (± 1.43)	6.94 (± 1.67)	**0.003**

SD = Standard Deviation.

Table 3. Multivariate analysis of factors associated with splenomegaly.

	OR adjusted	95% CI		P-value
		Lower	Sup	
NSAIDs	0.209	0.060	0.729	0.014
Hepatomegaly	6.067	1.710	21.522	0.005
Malaria	15.626	6.608	36.951	< 0.001
Mean Hb level (g/dL)	1.038	0.605	10.202	0.971
Number of platelets More than 400	0.488	0.202	0.786	0.041
Hemoglobin fraction F]0; 10]	2.266	1.632	8,120	0.039
Hemoglobin S fraction Over 90	0.111	0.019	0.646	0.015

NSAIDS: Non-steroidal anti-inflammatory drugs.

patients with an average age of 21 and 24.7 years [5] found respective prevalences of 26.8% and 21%. These values suggest a lower frequency than that observed in our study in pediatric patients. Moreover, in 2004, Awotua *et al.* during an ultrasound study conducted on 100 homozygous Nigerian children aged 6 to 15 years revealed splenomegaly in 27% of them [12]. This difference in prevalence is attributable to the older ages in the Nigeria series; older subjects have most often undergone autosplenectomy following multiple splenic infarctions. The same is true in the Middle East where the prevalence of splenomegaly is lower in series made up of subjects older than ours. Inati *et al.* in 2007, found splenomegaly in 28.9% of patients in a Lebanese series with an average age of 18 years [13]. The high prevalence of splenomegaly, 80%, found by Russo-Mancusco *et al.* [14] in a series of 518 cases of heterozygous HbS -beta-thalassaemia in Italy, is linked to the preponderance of heterozygous forms in this region. Indeed, in Jamaica, GR Serjeant *et al.* [15] have carried out work on the comparison between sickle cell disease S Beta-0 Thalassemia and homozygous sickle cell disease. They found that persistence of splenomegaly is more common in patients in the first group. This persistence could come from less intravascular sickling in these heterozygotes, linked to the decrease in the average corpuscular concentration of hemoglobin S. In our series, splenomegaly was more common in SC composite heterozygous patients (100%) than in homozygous (32.1%). The frequency of splenomegaly in heterozygous SC patients in our series was higher than the prevalence of 68% in heterozygous SC patients reported by Adjenou *et al.* [16] in Togo, in 2006. The greater frequency of splenomegaly in heterozygous SC patients in our study could be explained by the rarity of this phenotype in Central Africa, resulting in a low representativeness of this group (1% of our population of study).

Splenomegaly increased in frequency, from the age group of 6 months to 6 years (34.3%), to that of 6 to 10 years (40.3%) before decreasing from 10 to 16 years (25.4%). These findings agree with the data of Diagne *et al.* [9] in 2010 in Senegal, for whom the frequency of splenomegaly increased from the age group of 0 - 5 years to that of 6 - 10 years before decreasing thereafter. The same is true in India where Mukherjee *et al.* [17] found frequencies of 24.7% from 0 to 4 years old, 35.1% from 5 to 9 years old and 13.6% from 10 to 15 years old. These values are opposed to those of the literature where some authors [8] claim that complete splenic atrophy occurs in homozygous SS sickle cell disease at six years, following the congestive phase of the early years. Several hypotheses could explain this discrepancy. First, it is highly probable that many of the homozygous SS subjects in our study, carriers of splenomegaly, are actually compound heterozygotes. Note, for example, that the association SS—alpha thalassemia has the same tracing as homozygous sickle cell disease SS during conventional electrophoresis of hemoglobin at alkaline and acid pH; however, almost all of our patients were diagnosed from the results of conventional electrophoresis of hemoglobin at alkaline pH. Splenomegaly is more common in the association SS—alpha thalassemia than in homozygous sickle cell disease. Second, the existence of factors is likely to reduce the sickling of red blood cells and therefore the frequency of splenic infarctions in our study population. These include regular monitoring, educating patients to avoid factors that trigger sickling (cold, high altitudes, sustained and prolonged effort, etc.) and taking synthesis inducers of Hb F such as hydroxyurea. Thirdly, the mean age of the inaugural consultations in our population was 2.9 ± 2.49 years. Inaugural consultations were an exclusion criterion in our study. This could have led to a selection bias, thus favoring the age group of 6 to 10 years. This hypothesis seems unlikely to us, because it is absent from the series of Diagne *et al.* [9] and Mukherjee *et al.* [17].

Clinically, PS1 and PS0 sickle cell patients had several points in common. These included pallor, poor vaccination status, frequency of annual consultations and transfusions, chronic complications of sickle cell disease and the actual adoption of certain therapeutic measures (hyperhydration, antibiotic therapy and taking hydroxyurea). This corroborates the findings of GR Serjeant *et al.* [15], for whom, apart from splenomegaly, all the other clinical parameters were similar in the two groups of the series studied. However, sickle cell disease is characterized by a great variability of clinical and biological expressions which depend on modulating genetic and environmental factors. The presence of abdominal scarification scars strongly represented in PS1 (50.7% vs 19.4% $p < 0.001$) in our series is proof of this. In Cameroon, splenomegaly, commonly called "corner belle" meaning "at the edge of the abdomen", is a "disease" treated by traditional healers because many parents, out of ignorance, initially seek care from traditional healers. These healers perform abdominal scarifications whose purpose would be to extirpate the "bad blood" and to heal the "corner belle".

In our study, the analysis of clinical data showed a low frequency of va-

so-occlusive crises in patients with splenomegaly compared to patients without splenomegaly (48.48% vs 52.56%). The same fact had been described in Nigerian children by Adekile [10]. Like them, we also noted a greater frequency of episodes of severe acute anemia in cases of splenomegaly. We found hepatomegaly in 23.9% of PS1 subjects. This percentage is low compared to the 71.9% found by Balci *et al.* [18] in 2008 in Turkey. This difference could be related to the technique used. Indeed, Balci *et al.* used ultrasounds while we palpated the abdomen of the patients. Most patients had splenomegaly at the second stage according to Hackett classification (Hackett stage 2). This represented 56.7% of all splenomegaly observed. This corroborates the results of Sangare *et al.* [19] where 87.5% of patients had Hackett stage 2 splenomegaly. The splenomegaly seems more moderate in the association SS—alpha thalassemia.

In our series, PS1 were subject to more hospitalizations. The frequent reason for hospitalizations was severe anemia. On the other hand, the PS0 had frequent hospitalizations for vaso-occlusive crises and infections. These results contradict those of Diagne *et al.* [9] in Senegal. In his series, there was no significant difference between the frequencies of hospitalizations. This difference in results would be due to a larger sample in Senegal (889 vs 201) and a longer study duration (14 years vs 4 months).

Biologically, the hematological profile of sickle cell disease associated with splenomegaly in our study shows average hemoglobin and platelet levels lower than those of sickle cell patients without splenomegaly. These results corroborate those found by Ranque *et al.* [5] in 2017 and Adeodu *et al.* [20]. The simultaneous presence of hemoglobin S and A outside any context of recent blood transfusions, with the percentages of HbS much higher than those of HbA in six of our patients, suggests the existence in our environment of other forms of sickle cell disease. It could be a composite $\beta S/\beta+$-thalassemia or $\beta S/\delta^{\circ}\beta+$-thalassemia heterozygosity according to Zertal-Zidani *et al.* [21] or an association with an alpha triplication according to Steinberg *et al.* [22].

The higher hemoglobin F level in our patients who had splenomegaly is in favor of the role it would play in the persistence of splenomegaly during sickle cell disease [22]. This result was similar to that found by Diagne *et al.* in 2010 in Senegal [9]. Apart from the persistence of hemoglobin F, an associated alpha thalassemia trait would constitute a major etiological factor for the persistence of splenomegaly, as is the case in sickle cell patients in Congo [23] and India [17].

The rapid diagnostic test of malaria allowed us to find 74.6% of patients with splenomegaly (PS1) who had malaria. This value is higher than the 53% found by Mariam *et al.* [24] in Mali in 2009. This difference could be explained by the difference in the sensitivity of the tests chosen (TDR vs. thick film) and the study population. In Mali, Mariam *et al.* were interested in sickle cell patients in general, here the percentage of 74.6% of malaria infestation is observed in sickle cell patients with splenomegaly. In sub-Saharan Africa the persistence of splenomegaly is classic. In addition to the role of alpha-thalassemia and the persistence of hemoglobin F linked to the haplotype, malaria infestation would contribute to

the increase in volume of the spleen in patients with sickle cell disease living in endemic areas [25] [26] [27]. Indeed, an overactive malarial splenomegaly is one of the main causes of massive splenomegaly in tropical regions. Its pathogenesis is related to an aberrant immunological response to repeated plasmodial infestations, resulting in an enlarged spleen sometimes associated with secondary hypersplenism [27].

Factors associated with splenomegaly were: malaria, hepatomegaly, number of platelets, use of nonsteroidal anti-inflammatory drugs, fraction of hemoglobin F and fraction of hemoglobin S.

Our study reports NSAIDS as a factor associated with decreased risk for splenomegaly OR = 0.209 (0.060 - 0.729). However, several drugs have been reported to cause splenomegaly through several mechanisms [28]. They may cause neutropenia and predispose to infections. In the fight against these infections, splenic enlargement may result [29]. Furthermore, drugs may cause hemolysis. Increased hemolysis will therefore recruit the spleen and splenomegaly will result [29]. Though not specifically with NSAIDS, several studies relative to drug-induced hemolytic anemia (DIHA) in sickle cell patients [30] [31] [32] are available. Use of NSAIDs may reduce duration of sickle cell crisis by reducing pain, therefore halting the sickling cascade and may give an explanation for the findings in our study. Malaria however, is a well-known risk factor for splenomegaly. Malaria can cause an array of changes in the spleen ranging from mild enlargements to life-threatening splenomegaly [27] [33]. In our study, if a sickle cell patient had splenomegaly, he was 15 times more likely to also have malaria. This is in accordance with other studies. For example, Eleonore *et al.* [33] in Cameroon, 2020, reported a prevalence of splenomegaly at 25% in SCD patients with malaria versus 17% without malaria. It will be expected that a patient with splenomegaly also has hepatomegaly as these are both parts of the reticuloendothelial system and react similarly to hemolysis, infections and hematological disorders [34]. In a study carried out in Nigeria, both hepatomegaly and splenomegaly occurs in 4 out of every 10 sickle cell patient which is similar to what we obtained in our study (3/10). Splenomegaly more likely associated with thrombocytopenia as abnormal sickled RBCs together with platelets are trapped in the splenic circulation and cause splenic enlargement [34] [35]. Our study reports a decreased association between platelets > 400,000 cells/uL and splenomegaly. This has been reported similarly in literature. Generally, sickle cell patients with splenomegaly have associated thrombocytopenia especially in cases of acute sequestration crises [36]. High hemoglobin F (HbF) levels have been associated with persistent splenomegaly [37]. In our study, patients with HbF (0 - 10%) had twice increased probability of having splenomegaly. This may be a bias since Hb F has a protective role against sickling. Less sickling will imply less risk of autosplenectomy. In our sample, patients with autosplenectomy were not identified and could have been classified as PS0 erroneously. This brings bias because the spleen is not in the same state of function as for other patients [38]. Conversely a high level of HbS (>90%) was found to be less associated with splenomegaly.

This result is biased because only 0.01% (2/206) patients had a genotype other than HbSS.

Splenomegaly is associated with several factors, investigated and non-investigated in the current study. It's a condition that is painful and sometimes becomes life-threatening. More studies with more robust methodologies, longer follow-up, outcome determination and a wider sample need to be conducted for us to prevent and adequately manage sickle cell disease patients with splenomegaly.

5. Conclusion

Splenomegaly is common in 3/10 patients with sickle cell disease. It is significantly associated with taking NSAIDs, hepatomegaly, malaria, platelets over 400.00, HBF fraction < 10% and HbS fraction > 90%. Further studies are needed to confirm or invalidate these associated factors and to know the morbidity and mortality associated with splenomegaly in patients with sickle cell disease.

Current State of Knowledge on the Subject

- In Africa, the prevalence of splenomegaly in sickle cell disease was evaluated in Senegal at 17.5% by Diagne *et al. Plasmodium falciparum* infection and the haplotype would play a major role in the persistence of splenomegaly in sickle cell patients from sub-Saharan Africa compared to African-American populations.
- Splenomegaly gives rise to multiple relatively frequent and potentially serious complications in sickle cell disease, such as splenic sequestration crises, rupture of the spleen, hypersplenism and splenic abscesses.
- In Cameroon, data are almost non-existent. Therefore, we proposed to conduct this study, the general objective of which is to determine the prevalence of splenomegaly and to study the associated factors in subjects suffering from sickle cell disease at the Mother and Child Center of the Chantal Foundation. BIYA

Contribution of Our Study to Knowledge

- The prevalence of splenomegaly in our sample was 35.2%.
- Patients with splenomegaly more frequently had scarification, abdominal distension, hepatomegaly and were less jaundiced.
- The factors associated with splenomegaly in patients with sickle cell disease were NSAIDs use, hepatomegaly, malaria, platelets over 400.00 cell/uL, HBF fraction < 10% and HbS fraction > 90%.

Authors' Contributions

HD, HED, KOJ-PO and N-SM designed the study. HD and N-SM wrote the protocol. HD, HED, KOJ-PO and N-SM reviewed the protocol. HD collected and analyzed the data. N-SM supervised the study at every stage. HD and MMLE wrote the article. HD, CNS, MMLE, NCN, N-SM edited the article until submis-

sion for publication. All authors have given their consent for the submission of the article.

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Conflicts of Interest

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

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