

Hematological and Biochemical Profile of Sickle Cell Patients in Critical and Inter-Critical Periods in Brazzaville, Republic of Congo

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Abstract

Introduction: Sickle cell disease is a public health problem in the Republic of Congo where the prevalence of sickle cell trait is estimated at 1.25%. The objective of this study is to describe the variations of hematological and biochemical parameters of hemolysis in sickle cell patients in critical and inter-critical periods. **Methods:** This is a descriptive cross-sectional study including sickle cell patients followed regularly at the National Reference Center for Sickle Cell Disease (CNRDr) from November 2019 to March 2020. A sample of 167 patients (sickle cell subjects in crisis and in steady state as well as control subjects) was randomly selected during the study period. The blood count was performed using a Sysmex-XN 350 automated system and the biochemical parameters were determined using the Cobas e 311 automated system. Statistical analysis was performed with SPSS version 22 software. **Results:** The study showed that the mean cholesterol level in controls was 4.16 ± 0.77 ul compared with 9.64 ± 4.34 ul in sickle cell crisis subjects. Hb and HCT levels were significantly higher in controls compared with sickle cell subjects in crisis. During crisis, total bilirubin, direct bilirubin, triglycerides, LDH, AST, and CRP were significantly elevated. Hematological parameters such as Hb and HCT were elevated in controls, while the mean WBC value and RET were higher in sickle cell patients in steady state. The mean values of the biochemical parameters were higher in sickle cell patients in steady state. **Conclusion:** Evaluation of the influence of sickle cell trait on biochemical and hematological parameters showed significant differences between sickle cell and control subjects.

Keywords

Sickle Cell Disease, Hematological Parameters, Biochemical Parameters, Critical and Inter-Critical Period Brazzaville

1. Introduction

Sickle cell disease (SCD), also known as sickle cell anemia, is a hereditary disease characterized by a particular abnormality of hemoglobin S (HbS) which originates from a point mutation of the β -globin gene located on chromosome 11 at the 6th codon of exon I (GAG \rightarrow GTG) resulting in the replacement of glutamic acid by a valine [1] [2] [3] [4]. SCD is the most common genetic disease in the world, is mainly observed in black people. It is therefore a real public health problem in Africa where its prevalence varies from 10% to 40% of gene carriers depending on the region [5]. In the Republic of Congo, the prevalence of sickle cell disease in its homozygous form is 1.25% [6] [7]. The natural history of homozygous sickle cell disease is marked by acute and chronic complications whose distribution varies according to age [7]. Thus, acute complications consisting of intense painful attacks, deglobulation attacks and infections are the most frequent complications in children [8]. In adults, in addition to acute complications, chronic complications are observed and dominate the clinical picture [8], leading to metabolic disturbances, the characteristics of which in sub-Saharan Africa are poorly reported [4] [9]. Sickle cell disease is a truly systemic pathology, exposing the patient to numerous complications, including ischaemic disorders due to the lack of oxygenation of tissues. This results in organ damage, particularly to the liver and kidney [10] [11] [12], may be manifested by disturbances in the metabolism of certain biochemical variables. Clinical and epidemiological studies have shown the responsibility of total cholesterol, especially LDL-cholesterol, and lower HDL-cholesterol lowering of HDL-cholesterol. There is controversy about the values of biochemical parameters especially in sickle cell disease patients. According to Rahimi *et al.* [13], subjects with sickle cell disease have increased HDL-cholesterol, whereas subjects with homozygous sickle cell disease have a lower total cholesterol concentration compared to normal subjects (Hb AA) and subjects with sickle cell disease (Hb AS). For Ephraim *et al.* [14] and Gueye Tall *et al.* [15], a decrease in total cholesterol and HDL cholesterol was observed in homozygous and heterozygous sickle cell disease subjects compared to non-sickle cell subjects. Magalhães Aleluia *et al.* [16] reported an increase in total cholesterol, HDL cholesterol and LDL cholesterol and a decrease in triglycerides. Other authors have found a decrease in HDL cholesterol and a simultaneous increase in LDL cholesterol, indicating potential biomarkers for disease severity [17] [18]. The aim of this study is to describe the variations of hematological and biochemical parameters of hemolysis in sickle cell patients in critical and inter-critical periods.

2. Methods

2.1. Study Design and Population

This is a cross-sectional and descriptive study including sickle cell patients followed regularly at the National Reference Center for Sickle Cell Disease “Antoinette Sassou N’Guesso” (CNRDr) in critical and inter-critical periods as well as controls subjects covering the period from November 2019 to March 2020. A total of 67 sickle cell patients in crisis period and 68 in steady state were included. The critical state was clinically defined by vaso-occlusive crises: abdominal, bone, thoracic, priapism, deglobulation crisis and/or infection requiring immediate management. For the control population we selected 40 non-sickle cell patients free of any other infections. The purpose of the study was explained to the participants in the language of their choice before the study and informed consent was obtained from them. Individuals who could not give consent were excluded from the study.

Inclusion criteria were:

- **Sickle cell patients in the inter-critical period:** Absence of vaso occlusive crisis episodes and/or intercurrent diseases in the 4 weeks prior to the study; no hospital admissions in the 3 days prior to the study; no blood transfusions in the 4 months prior to the study;
- **Sickle cell patients in critical period:** Sickle cell patient followed at the CNRDr and admitted in crisis state before any care;
- **Controls:** Non-sickle cell patient, patients/guardians who have given consent

Non-inclusion criteria were: Sickle cell patient in gestational state; sickle cell patient/controls refusing to participate in the study and blood samples not usable.

2.2. Sample Collection

5 ml of blood was collected by venipuncture into BD vacutainer tubes containing the anticoagulant EDTA for the determination of hematological parameters and into BD dry vacutainer tubes for the determination of biochemical parameters. After centrifugation at 3000 rpm for five minutes, the sera were aliquoted into eppendorf tubes and stored at minus 80 degrees Celsius at the National Public Health Laboratory for delayed analysis of biochemical parameters.

2.3. Biological Analyses

The blood count was performed using a Sysmex—XN-350 (Sysmex Corporation, Kobe, Japan) at the CNRDr laboratory within minutes of sampling for patients in crisis, 2 hours later for sickle cell patients in steady state and 6 hours before sampling for controls.

The determination of CRP was performed by immunoturbidimetric method, LDH-cholesterol, triglycerides, ASTL by enzymatic colorimetric method, for total and direct bilirubin by diazoreaction method thanks to the Cobas Roche e311 (Hitachi) multiparametric automaton.

2.4. Statistical Analysis

Statistical analyses of the data were performed with SPSS version 22 software. The different groups were compared using the Student t test. The significance level used was 5% ($p < 0.05$).

3. Results

3.1. Demographic Parameters of SCD Subjects and Controls

The majority of participants (53.7%) in this study were female. Females were predominantly represented in the sickle cell crisis (59.7%) and steady state (57.4%) groups. The age group 6 - 10 years (26.9%) was the most represented (**Table 1**).

3.2. Comparison of Haematological and Biochemical Parameters in Sickle Cell Patients in Crisis and Controls

The mean values of hematological and biochemical parameters between sickle cell subjects in crisis and controls are presented in **Table 2**. The mean White Blood Cell (WBC) level in controls was about 4.16 ± 0.77 ul versus 9.64 ± 4.34 ul in sickle cell subjects in crisis. The Mean of hemoglobin (Hb) and hematocrit (HCT) values were significantly higher in controls compared with sickle cell subjects in crisis. In patients in crisis, the reticulocyte count (RET), total bilirubin, direct bilirubin, triglycerides, lactate déshydrogénase (LDH), Aspartate aminotransférase (AST) and C-Reactive Protein (CRP) were significantly elevated compared to the levels observed in controls.

3.3. Comparison of Hematological and Biochemical Parameters in Sickle Cell Patients in Steady State and Controls

Table 3 shows that the mean levels of hematological parameters such as Hb and HCT were elevated in controls, while the mean WBC value and RET were higher in sickle cell patients in steady state. The differences between the means of the

Table 1. Demographic parameters of SCD subjects and controls.

Parameters	Controls (N = 40) n (%)	Crisis (N = 67) n (%)	Steady state (N = 68) n (%)	Total n (%)
Sexe				
Female	15 (37.5)	40 (59.7)	39 (57.4)	94 (53.7)
Male	25 (62.5)	27 (40.3)	29 (42.6)	81 (46.3)
Age				
6 month - 5 year	5 (12.5)	22 (32.8)	14 (20.6)	41 (23.4)
6 - 10 year	10 (25.0)	19 (28.4)	18 (26.5)	47 (26.9)
11 - 15 year	6 (15.0)	12 (17.9)	9 (13.2)	27 (15.4)
16 - 20 year	9 (22.5)	10 (14.9)	15 (22.1)	34 (19.4)
21 - 57 year	10 (25.0)	4 (6.0)	12 (17.6)	26 (14.9)

Table 2. Hematological and biochemical parameters in sickle cell patients in crisis and in controls.

Parameters	controls	Crisis	p
WBC/10 ³ /ul	4.16 ± 0.77	9.64 ± 4.34	<0.001
Hb/g/dl	14.16 ± 1.68	4.35 ± 1.13	<0.001
HCT%	38.49 ± 5.31	14.85 ± 3.96	<0.001
RET%	0.87 ± 0.12	12.21 ± 9.27	0.001
CRP/mg/l	4.05 ± 0.89	19.63 ± 29.01	0.001
AST mg/l	23.40 ± 6.57	38.45 ± 11.76	0.001
LDH mg/dl	52.36 ± 3.40	70.13 ± 16.78	<0.001
Triglycerides mg/dl	103.85 ± 6.37	160.51 ± 35.70	<0.001
Total bilirubin mg/dl	0.87 ± 0.77	5.31 ± 3.21	<0.001
Direct bilirubin mg/dl	0.06 ± 1.68	1.22 ± 0.15	<0.001

LDH: lactate déshydrogénase; WBC: White Blood Cell; Hb: Hemoglobine, HCT: hématocrite; RET: Reticulo-cyte, CRP: C-Reactive Protein, AST: Aspartate aminotransférase.

Table 3. Hematological and biochemical parameters in sickle cell patients in steady state and in controls.

Parameters	controls	steady state	p
WBC/10 ³ /ul	4.16 ± 0.77	8.55 ± 3.01	<0.001
Hb/g/dl	14.16 ± 1.68	7.24 ± 1.62	<0.001
HCT%	38.49 ± 5.31	21.15 ± 4.60	<0.001
RET%	0.87 ± 0.12	10.74 ± 4.93	0.30
CRP/mg/l	4.05 ± 0.89	10.35 ± 1.98	<0.001
AST	23.40 ± 6.57	31.34 ± 10.63	0.001
LDH mg/dl	52.36 ± 3.40	37.34 ± 21.45	0.001
Triglycerides mg/dl	103.85 ± 6.37	141.24 ± 30.50	<0.001
Total bilirubin mg/dl	0.87 ± 0.77	2.50 ± 3.21	<0.001
Direct bilirubin mg/dl	0.06 ± 1.68	0.74 ± 0.15	<0.001

different parameters were statistically significant. The means of the biochemical parameters (AST, CRP, LDH, Triglycerides, Total and Direct Bilirubin) were significantly higher in sickle cell patients in steady state.

3.4. Clinical Complications in Sickle Cell Patients in Crisis

The majority of sickle cell subjects in crisis had vaso-occlusive crises (VOC). Of these patients 30.9% had bone CVO's versus only 4.4% had thoracic CVO's. 5.8% of men in crisis had priapism (Table 4).

4. Discussion

In the present study, CRP as well as WBC levels significantly elevated in sickle

Table 4. Clinical complications in sickle cell patients in crisis.

Complications	Sckell cells patiens (crisis)	
	n	%
Abdominal CVO	15	22.1
Bone CVO	21	30.9
Thoracic CVO	3	4.4
CAD	14	20.6
Infection	11	16.2
Priapism	4	5.8
Total	68	100

CVO: vaso occlusive crisis; CAD: acute deglobulation crisis.

cell subjects compared to control subjects. These elevated levels could be explained by the fact that sickle cell disease is an inflammatory disease with leukocytosis as one of the markers [15]. Thus, the increase in CRP confirms that homozygous sickle cell subjects are prone to numerous attacks [15]. Similar results were found by Monnet *et al.*, [19] and Benjamin *et al.*, [19]. The mean value of LDH found in sickle cell patients in stationary phase compared to controls is in agreement with the results reported by Tshibumbu *et al.* in 2019 [20]. This result would be due to the activity of lecithin cholesterol acyltransferase (LCAT) because for this enzyme the preferential substrate is LDH in the human species [21]. In contrast to sickle cell subjects in steady state, a high level of LDH was observed in sickle cell subjects in crisis compared to controls. This observation is similar to that reported by Mokondjimobe *et al.* in 2012 [22]. In that study, the mean total bilirubin level was higher in sickle cell subjects (in crisis and steady state). These results are in agreement with other works [23] [24]. Furthermore, the high direct bilirubin level in sickle cell subjects showed that these subjects hemolyzed twice as much as control subjects. This result is similar to that of Ballas and Marcolina [25]. Significantly high triglyceride values were observed in sickle cell subjects in crisis and in steady state. These results would be due to the decrease in lipoprotein lipase activity, which is linked to the oxidative stress process [21]. Many epidemiological studies show that hypertriglyceridemia is independently related to cardiovascular risk in both men and women. These studies show that hypertriglyceridemia can have atherogenic and thrombogenic consequences suggesting that the homozygous sickle cell patients in our study would be exposed to cardiovascular risk [26]. The results of our study show that both crisis and steady state patients have lower mean HCT and Hb levels than controls, which is comparable to other studies [27] [28]. The effects of anemia, infection, and hemolysis could explain the lower values observed in crisis patients compared to steady state patients. Infection is, as confirmed by other studies, an important etiological factor [29] [30]. Priapism is rare. The majority of our patients had CVO. 29.16% of the CVOs encountered had bony expression.

This result is similar to that of ELIRA *et al.* [31]. From January 1995 onwards, these crises have practically disappeared in the series of patients on hydroxyurea. It was found that these attacks were less paroxysmal and less unpredictable [31].

5. Conclusion

The evaluation of the influence of the sickle cell trait on the biochemical and haematological parameters of inflammation represented by the serum concentrations of LDH, triglycerides, bilirubins, WBC, Hb, RET, HCT and the serum protein of inflammation (CRP) shows significant differences between sickle cell subjects (in crisis period in steady state) and control subjects.

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Conflicts of Interest

The authors declare no conflicts of interest.

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