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Evolutionary Profile of Drepanocytic Patients Followed at the National Drepanocytosis Reference Centre (CNRDr) Congo Brazzaville

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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 aim of this study was to establish the profile of sickle cell patients regularly followed at the CNRDr. Methods: This is a descriptive cross - sectional study including sickle cell patients regularly followed at the National Reference Centre for Sickle Cell Disease (CNRDr) from November 2019 to March 2020. A sample of 127 patients was randomly selected during the study period. Blood counts were performed with a Sysmex - XN 350 automated system and CRP was determined with the Cobas 311 automated system. Statistical analysis was performed with SPSS version 22 software. Results: The study showed that the disease was diagnosed in 31.5% of the sickle cell patients as a result of the hand - foot syndromes. Sickle cell disease was discovered as a result of prenatal diagnosis in only 1.6% of patients.87.4% of patients came from the department of Brazzaville and 12.6% from the interior of the country. The patients included in our study were transfused on average 1.78 times per year with a standard deviation of 0.80 (1.78±0.80). The number of OVCs and hospitalizations was 2.41±0.40 and 2.90±1.02 respectively. The majority of subjects made 1.9±1.02 visits per year. The WBC was 10.36±4.49 in men and 7.93±2.49 in women. Haematocrit (HCT) and reticulocytes (RET) were significantly higher in men (19.13±5.44 and 0.29±0.12, p<0.05) than in women. The mean CRP was higher in women. Conclusion: This study shows that the management of sickle cell disease in the Republic of Congo is improving. The problem being well identified, it is imperative to create specialised units for the management of this haematological condition in other departments of the country.***

Keywords: Sickle cell disease, haematological parameters, biochemical parameters, critical and inter - critical period Brazzaville

1. Introduction

Sickle cell anaemia or sickle cell disease is the leading genetic disease in the world, affecting more than 50 million people and affecting more than 300, 000 to 500, 000 children each year, of whom 400, 000 are born in Black Africa [1] [2]. In Black Africa, which is the main primary focus of the disease, the prevalence varies between 15 - 45% [3] [4]. In Congo, according to a study byDjemo Tati et al, as in some countries in the sub - region, the prevalence of the sickle cell trait varies from 20.78% to 23.53% and is estimated at 1.25% of children born with the homozygous form (SS) [5] [6]. Hemoglobin disorders are a major public health problem, mainly among black people, and account for about 9% of deaths in children under 5 years of age in Africa [7] [8]. This condition results from a point mutation in the β - globin gene located on chromosome 11 at the 6th codon of exon I (GAG → GTG) leading to the replacement of glutamic acid by valine [9] [10] [11] [12] which induces polymerisation of haemoglobin S (Hb S), leading to haemolysis and vaso - occlusive events [13] [14], thus presenting a highly variable clinical and biological picture [15], which leads to complications such as infarcts in various organs. Therefore, on the basis of analyses of point mutations whose association determines the haplotype, five main foci of sickle cell disease have been described, confirming the multi - centre origin of the mutation: the Arab - Indian, Benin, Cameroon, Bantu or Central African (CAR) and Senegal haplotypes, which correspond respectively to specific geographical areas [16]. The literature reports a high incidence of clinical complications in patients carrying the Bantu gene compared to others [17] [18], mainly in Central Africa [19] [20].

In the Republic of Congo, the severity of the disease is marked by haemolytic complications associated with profound anaemia and biological factors indicating severe morbidity [21]. Few studies offer us the evolutionary profile of sickle cell patients, so we propose to describe the sociodemographic and evolutionary aspects of the disease with the aim of better management.

1.1 Patients and Methods

Patients: we recruited 127 sickle cell patients regularly followed at the National Reference Centre for Sickle Cell Disease and Rare Diseases "Antoinette SASSOU N'GUESSO" (CNRDr) in Congo covering the period from November 2019 to March 2020. Written and/or oral informed consent was obtained from adults and parents/guardians of the recruited children.

Method: This is a descriptive study of the epidemiological, clinico - biological and evolutionary aspects of SS sickle cell patients followed regularly at the Sickle Cell Reference Centre. Data on the history of their pathologies were collected from the patients' files and other information was completed during the study period. Socio - demographic variables were age, sex and origin in relation to the country department. The clinico - biological variables were age of diagnosis, circumstances of discovery of the disease, history of stroke, priapism, cholecystectomy and splenectomy; frequency of hospitalisations, frequency of blood transfusions, frequency of vaso - occlusive crises (VOC) and biologically we measured CRP and haemogram parameters.

1.2 Sample Collection

5 ml of blood was collected by venipuncture into BD vacutainer tubes containing anticoagulant EDTA for the determination of haematological parameters and into dry BD vacutainer tubes for the determination of the biochemical parameter. 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 the biochemical parameter.

1.3 Biological analyses

The haemogram was performed using a Sysmex - XN - 350 (Sysmex Corporation, Kobe, Japan) and the CRP determination was performed by the immunoturbidimetric method, using the Cobas Roche e311 (Hitachi).

1.4 Statistical analyses

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

2. Results

A total of 127 patients (62 in crisis and 65 in stable state) were included in this study.70 were female (55.1%) and 57 were male (44.9%), giving a sex ratio of 0.81. The mean age of the study population was 19.55±12.84 years with extremes ranging from 1 to 60 years. The distribution of patients by age group shows that the age group 10 - 19 years (29.1%) was the most represented (Table I).

Table I: Socio - demographic characteristics of patients

Socio - demographic variables	Patients (N=127)	
	N	%
Gender		
Male	70	55.1
Female	57	44.9
Age groupe		
<10	32	25.2
10 - 19	37	29.1
20 - 29	31	24.4
30 - 39	15	11.8
≥40	12	9.4

Table II shows the clinical parameters of sickle cell patients. The disease was diagnosed in 31.5% of the sickle cell patients as a result of hand - foot syndromes. Sickle cell disease was discovered as a result of prenatal diagnosis in only 1.6% of patients.

Table II: Circumstances of discovery

Circumstances of discovery	n	%	Average age (months)
Hand - foot syndrome	40	31.5	4.7±1.2
Icterus	5	3.9	6.8±3.4
CVO	27	21.3	7.1±4.1
Anemic crisis	19	15.0	9±3.1
Priapism	14	11.0	11.2±5.4
Sans souvenir	8	6.29	14.2±1.4
Routine check - up	7	5.5	8.3±4.1
Infectious Syndrome	5	4.0	9±3.1
Screening	2	1.6	7±2.4
Total	127	100.0	

According to origin, 87.4 % of patients came from the department of Brazzaville against 12.6 % from the interior of the country (table III). Table IV shows the average number of transfusions, CVOs and hospitalisations per year. The patients included in our study were transfused on average 1.78 times per year with a standard deviation of 0.80 (1.78±0.80). The number of CVOs and hospitalizations was 2.41±0.40 and 1.9±1.02 respectively. The majority of the patients made between 3.02±0.80 visits per year.

Table III: Departments

Departments	n	%
LIKOUALA	1	0, 8
NIARI	3	2, 4
POINTE - NOIRE	5	3, 9
BOUENZA	3	2, 4
SANGHA	2	1, 6
CUVETTE OUEST	1	0, 8
PLATEAUX	1	0, 8
BRAZZAVILLE	111	87, 4
Total	127	100, 0

The haematological and biochemical parameters of the patients according to gender are presented in Table V. The white blood cell count (WBC) was 10.36±4.49 in men and 7.93±2.49 in women. Comparison of the mean WBC levels showed a statistically significant difference ($t=3.51$, $p<0.05$). Haematocrit (HCT) and reticulocytes (RET) were significantly higher in men (19.13±5.44 and 0.29±0.12, $p<0.05$) than in women. Comparison of other haematological parameters in both groups (males and females) showed no significant difference ($p>0.05$). The mean CRP was higher in females.

Table V: Biological Parameters

Biological parameters	Patients		*t*	P
	Females	Males		
WBC (10^3/ul)	7.93±2, 94	10.19±4, 34	3.51	0.001*
RBC (10^6/ul)	2.62±0, 85	2.78±0, 67	1.20	0.23
Hb (g/dl)	4.49±1.87	5.31±2.09	1.96	0.05
HCT (%)	16.77±5, 17	19.13±5, 44	2.22	0.03*
MCH (pg)	27.68±3, 58	27.28±3, 81	0.56	0.57
MCHC (g/dl)	35.01±4, 59	33.99±1, 97	1.31	0.19
RET (10^6/ul)	0.26±0.11	0.29±0.12	2.11	0.03*

RET (%)	10.23±5, 22	13.19±9, 21	0.38	0.70
CRP	15.07±1, 2	14.05±0.89	0.37	0.04

3. Discussion

Sickle cell disease is a genetic disease of autosomal recessive inheritance, linked to a qualitative abnormality in the structure of haemoglobin, which results in the formation of haemoglobin S (HbS) [7]. The aim of this study was to establish the profile of sickle cell patients regularly followed up at the CNRDr. In our study, the sex ratio was 0.81 in favour of the female gender. This female majority could be due to the high attendance of women at health facilities compared to men. This result is similar to that of Simo et al. in 2019 [22] on the follow - up of sickle cell patients. There were more subjects between the ages of 10 and 19 years. This result is thought to be due to the reduced life expectancy of sickle cell patients. This observation is contrary to that made by Yusuf et al. in 2015 in a study which showed a greater proportion of patients aged over 20 years [23]. This difference is thought to be due to the fact that consultations are free of charge at the CNRDr for anyone under the age of 12. Foot and hand syndrome was the main circumstance of discovery reported by the patients. Tshilolo L. [24] and Ya Pongombo Y. M [25] had also observed that foot - hand syndrome was the main circumstance of discovery. This observation is contrary to those of Girot et al who rather indicate CVO as the main syndrome at the discovery of the disease [26]. The majority of patients included in the study lived in Brazzaville. This result could be explained by the fact that the only centre for sickle cell disease patients is in Brazzaville, but also by the difficulty for patients from the interior of the country to travel to Brazzaville for treatment. The average number of visits is 3.02±0.80 per year, which is far from the recommendations of the French National Authority for Health (HAS) concerning the follow - up of patients with MDS [27]. It would therefore be important to educate sickle cell patients more on the issue, but also to facilitate their access to care by finding funding that will allow the costs to be amortized. The number of transfusions and the number of hospitalizations are respectively 1.78±0.80 and 1, 9±1, 02per year. This low rate is thought to be related to better patient management and effective treatment. Changes in haematological parameters may explain the complications observed in patients with sickle cell disease [7]. The mean MCV value was higher in men than in women. This result is similar to that reported by Nagose and Rathod [28], although no statistically significant difference was observed in our study ($p>0.05$). The study by Serjeant et al. however, found a higher MCV in women than in men [29]. High Hb and RBC levels were found in male patients compared to female patients. No significant difference was observed ($P >0.05$). These results could be explained by blood loss due to haematuria, repeated infections and nutritional deficiencies due to low socio - economic status [30]. Similar results have been reported by many authors [31], [32]. The mean MCHC was low in men. This average is comparable to those obtained in several other studies [33], [34], [35]. In the present study, CRP levels were high in sickle cell subjects. These high levels could be explained by the fact that sickle cell disease is an inflammatory disease of which leukocytosis is one of the markers [36]. Thus, the increase in CRP confirms that homozygous sickle cell subjects are prone to numerous attacks [36]. Similar result were found by Monnet et al, [33].

4. Conclusion

This study reveals that the management of sickle cell disease in the Republic of Congo is improving. As the problem is well identified, it is imperative to create specialised units for the management of this haematological condition in other departments of the country, but also a large - scale public awareness campaign, the involvement of the State and the support of partners are essential in order to improve the quality of care for sickle cell patients.

5. Conflicts of interest

The authors declare no conflict of interest.

6. Acknowledgments

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