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Impact of Factors Associated with Chronic Complications in the Life of Sickle Cell Patients in Kinshasa

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Abstract

Context: Studies describing the factors associated with chronic complications and their impact on the life of adult sickle cell patients are rare. **Objective:** Contribute to improving the care of sickle cell patients in Kinshasa through the analysis of the impact of factors associated with chronic complications of sickle cell disease. **Method:** This is a cross sectional analytical study. **Results:** This research was carried out in a cross-sectional manner on 230 sickle cell patients aged at least 15 years recruited at the Center for Mixed Medicine and SS anemia and also in three associations of sickle cell disease patients in Kinshasa. The median age was 23.55 years (extremes 1543 years), the majority of whom were female (58.3%), with a sex ratio M/F = 0.72. Chronic complications were mainly infectious (47.2%), followed by hemolytic (27.6%) and ischemic (25.2%). Occupation, level of education, socioeconomic level (social class), and the presence and number of sickle cell siblings in the family were identified as potential factors for the occurrence of chronic complications. **Conclusion:** Sickle cell patients in Kinshasa have a low overall Quality of Life, particularly in its physical component, which is significantly affected by psychological limitations. Thus, improving the living conditions of sickle cell patients, better follow-up and accessibility to care should contribute to improving the quality of Life of sickle cell patients in DRC.

Subject Areas

Hematology

Keywords

Sickle Cell Disease, Chronic Complications, Associated Factors

1. Introduction

Sickle cell disease was declared a public health priority by the United Nations in 2008 and the WHO estimates that approximately 300,000 children are born each year with a serious hereditary hemoglobin disorder and that approximately 80% of these births occur in low- and middle-income countries [1].

Sub-Saharan Africa remains the most affected part of the continent. The frequency of carriers of sickle cell trait varies and can reach 40% within certain African populations. The frequency of sickle cell trait increased from 15% to more than 40% [2].

The Democratic Republic of Congo is the 3rd most affected country after India and Nigeria. It is estimated that 20 million Congolese (or 25% to 30% of the population) carry the sickle cell gene and can transmit the disease to their children. Up to 2% of children are born with sickle cell disease each year in the country. More than half of them die before the age of 5, due to lack of diagnosis [3]. An infant mortality rate, estimated at 127 per 1000 live births is among the highest in Africa [4]. Each year, there are approximately 32,000 - 48,000 births of children with sickle cell disease, *i.e.* 0.96% - 1.4%, and 2% of these newborns are homozygous [5]. According to reports from Ghana, an estimated 15,000 children are born with sick cell anemia each year [6].

Sickle cell disease combines three main categories of clinical manifestations with great variability of expression depending on the affected individuals. This is a susceptibility to bacterial infections; chronic hemolytic anemia with episodes of acute worsening; vaso-occlusive phenomena [7].

Under the term, major sickle cell syndrome is grouped with the clinical manifestations observed in cases of SS homozygosity and double heterozygosity SC, SD Punjab, thalassemic Sβ, SO Arab. Carriers of the S trait (AS heterozygous patients) are asymptomatic.

The progression of the disease is characterized by progressive multisystem damage which can result in the failure of one or more vital organs and which explains the diversity of chronic complications that can manifest from adolescence or adulthood [7] [8]. The Bantu, Benin and Cameroon haplotypes are those associated with a low hemoglobin F level and a high severity of sickle cell disease.

The criterion of survival or morbidity no longer appears sufficient to evaluate

medical progress, and the interest in taking into account subjective elements reflecting the patients' point of view is emerging [9] [10].

In the Republic Democratic of Congo, most studies are hospital-based, piecemeal and, moreover, no follow-up study from birth to adulthood has been carried out to highlight the link between the transitions to chronicity of acute complications. Organic, repetitive and inherent to the evolution of the life of the sickle cell patient, and their impact on the life of the adult sickle cell patient.

This is what motivates the present work based on the following main question: What are the factors that influence chronic complications and affect sickle cell patients living in Kinshasa?

To answer this question, we formulate the following hypothesis:

Poor access to healthcare services, ignorance of the mechanisms by which the disease occurs and insufficient care expose sickle cell patients to chronic complications responsible for reducing their life expectancy.

Goals

Main objective

Contribute to improving the care of sickle cell patients in Kinshasa through the analysis of the impact of factors associated with chronic complications of sickle cell disease.

2. Methods

Setting and Type of Study

The study was mainly carried out at the Center for Mixed Medicine and SS anemia (CMMASS) located in the urban center of the provincial city of Kinshasa and in the sickle cell support associations located in the city of Kinshasa. These are: Rézo drépano in the city center (ZS Gombe), le Cri du drépanocytaire to the east of the city (ZS Kimbanseke) and La Colombe to the west of the city (ZS Binza-Météo) whose choice was made randomly, based on the favorable responses obtained from the leaders of these associations. In the Democratic Republic of Congo

We carried out a cross-sectional analytical study from 1st July to August 7, 2021.

Study population

The study population consists of sickle cell patients aged 15 and over living in the city of Kinshasa in the Democratic Republic of Congo.

At the hospital, data were collected from patients hospitalized or undergoing routine consultation at the center. In the associations, the questionnaire was distributed to the members of the association during the various assemblies or during scheduled meetings with some of them.

Inclusion criteria

This is a systematic sample of all sickle cell patients who attended the CMMASS during the study period and of sickle cell patients who responded to the invitation launched by sickle cell support associations during the study period.

- Have homozygous (SS) or heterozygous (AS) sickle cell disease
- be at least 15 years old
- Not being in a sickle cell crisis

Exclusion criteria

We excluded all patients who had refused to participate in the study

Parameters of interest

➢ Type of sampling.

Sample size

The sample size was calculated from the Lorentz formula:

$n = \frac{t^2 X\, p(1-p)}{e^2}$, with:

n = required sample size, t = 95% confidence level (standard value of 1.96), p = prevalence of homozygous sickle cell trait in the DRC estimated between 1.6 and 2% (19), e = margin error at 5% (typical value of 0.05).

The minimum sample size was therefore:

$n = \frac{(1.96)^2 \times 0.02(1-0.02)}{(0.05)^2} = 30.12$ or 30 sickle cell patients.

In total, 44 patients were recruited in the SS Mixed Medicine and Anemia Center from July 4 to July 18, 2021 and 186 patients in the sickle cell associations of Kinshasa from 07/19/2021 to 08/06/2021

➢ Ethical considerations

A consent form was signed by each patient or by their legal representative for minor patients.

➢ Statistical analyzes

Analyzes were performed using the Wilcoxon-Mann Whitney test which is used to compare differences between two independent groups when the dependent variable is either ordinal or continuous, but not normally distributed.

The second one is Pearson's Chi2 test or Fisher's exact test, as appropriate, for quantitative and qualitative variables, respectively.

Data collection and organization

Sociodemographic data

The following variables were considered: age, sex, marital status, socio-professional category, level of study, neighborhood and municipality of residence, social class, number of brothers and sisters, position in siblings and the number of brothers and/or sisters with sickle cell disease per family.

Clinical data

They were collected in the form of semi-closed questions. The following variables were retained: the type of sickle cell disease from which the patient suffers, the age of discovery of the disease, the occasion of discovery of the disease, the reaction to the announcement of the diagnosis, the number of vaso-occlusive crises, the number of transfusions during the last 6 months preceding the survey, the number of hospitalizations during the last 6 months preceding the survey, the causes of occurrence of crises, the presence or absence of chronic complica-

tions, the type of chronic complications, follow-up outside of crises, reason for consultation, advice received regarding sickle cell status.

Biological data

Patients were invited to name the types of examinations carried out taking into account the proposals in the questionnaire: Hemoglobin, Thick Gout, Complete Blood Count + Sedimentation Rate, Biochemistry, and others.

Data analyzes

The collected data were recorded on SPHINX software and were processed and analyzed using R software.

Differences were considered at the 5% significance level.

3. Results

Table 1 taking into account the socio-demographic data and chronic complications, we have drawn up Taking into account socio-demographic data and chronic complications, we have drawn up Table 1 highlighting the different associations between the presence or absence of chronic complications. We see that the study involved 230 sickle cell patients, with a median age of 23.55 years, the youngest was 15 years and the oldest 43 years, the majority of whom were female 134 (58.3%), with one gender -M/F ratio = 0.72

the majority of patients with or without chronic complications are unemployed at 90.4% and 100% respectively ($p = 0.05$), with secondary education in a respective proportion of 53.2% and 66.7 % ($p = 0.010$) and an average socio-economic level, respectively 77.7% and 47.6% ($p < 0.001$). The proportion of having more than one homozygous sickle cell patient in the family is significantly higher in patients with chronic complications (48.9%) than in those without chronic complications.

Table 2 that incidental consultation was significantly the most representative circumstance of discovery whether for sickle cell patients with or without complications ($p < 0.001$). Furthermore, the rhythm of monthly crises was most common in sickle cell patients with chronic complications while the annual rhythm was found mainly in sickle cell patients without complications ($p = 0.036$).

Table 3 shows that chronic complications were mainly infectious (47.2%), followed by hemolytic complications (27.6%) then ischemic complications (25.2%).

Of the infectious complications, osteomyelitis was the most frequent complication with 34.6%, followed by septic arthritis (12.2%). Concerning hemolytic complications, gallstones were the most frequent (11.7%), followed by malleolar ulcers (11.2%). As for ischemic complications, they were dominated by osteonecrosis (17.6%).

Table 4, it appears that Hb (85%) and complete blood count (59.5%) were the biological examinations performed more significantly in patients without chronic complications than in those with chronic complications (respectively 36.2% and 30.3%).

Table 1. Sociodémographic profile according to chronic complications.

Variables	No complication (n = 42)	complications (n = 188)	p-value
Age (year), médian (EIQ)	24 (18 - 27)	22 (19 - 28)	0.673
Place of recruitment, n (%)			0.816
Extra hospital	35 (83.3)	151 (80.3)	
Intra hospital	7 (16.7)	37 (19.7)	
Gender, n (%)			0.294
Female	28 (66.7)	106 (56.4)	
Male	14 (33.3)	82 (43.6)	
Marital status, n(%)			0.478
Bachelor	38 (90.5)	168 (89.4)	
Free union	0 (0.00)	8 (4.3)	
Married	4 (9.5)	11 (5.8)	
Divorced	0 (0.00)	1 (0.5)	
Occupation, n (%)			**0.05**
Employee/Skilled worker	0 (0.0)	18 (9.6)	
unemployed	**42 (100)**	**170 (90.4)**	
Level of study, n (%)			**0.010**
Primary	1 (2.4)	39 (20.7)	
Secondary	**28 (66.7)**	**100 (53.2)**	
Higher/University	13 (30.9)	44(23.4)	
Postgraduate	0 (0.00)	5 (2.7)	
Social class, n (%)			**<0.001**
Disadvantaged	17 (40.5)	30 (15.9)	
Average	**20 (47.6)**	**146 (77.7)**	
Well-of	5 (11.9)	12 (6.4)	
Brother/Sister SS, n (%)	12 (28.6)	**92 (48.9)**	**0.026**
Siblingposition, médian (EIQ)	2 (1 - 4)	2 (1 - 4)	0.915
Number of SS Brother /Sister, médian (EIQ)	**0 (0 - 1)**	**0 (0 - 1)**	**0.016**

Table 2. The clinical profile depends of the presence of absence of chronic complications.

Variables	No complications (n = 42)	complications (n = 188)	p-value
Type SS, n (%)			1
Homozygous SS	35 (83.3)	156 (83.0)	
AS Hétérozygous	6 (14.3)	25 (13.3)	
S béta Thalassemia	1 (2.4)	4 (2.1)	

Continued

Do not know	0 (0.0)	3 (1.6)	
Circumstance of discovery of diagnosis, n (%)			**<0.001**
Complications of Sickle cell disease	9 (21.4)	23 (12.2)	
Chance consultation	**23 (54.8)**	**102 (54.2)**	
Hb Electrophoresis	10 (23.8)	31(16.5)	
Do not know	0 (0.0)	32 (17.1)	
Réactions to the announcement of the SS Diagnosis, n (%)			0.544
Refusal of Diagnosis	13 (31.0)	66 (35.1)	
Request a counter-expertise	12 (28.6)	44 (23.4)	
To go to church	6 (14.3)	19 (10.1)	
Traditional practitioner	5 (11.9)	13 (6.9)	
Do not know	6 (14.3)	46 (24.5)	
Seizure rhythm, n (%)			**0.036**
Annual	**23 (54.8)**	57 (30.4)	
Monthly	15 (35.7)	**89 (47.3)**	
Weekly	4 (9.5)	39 (20.7)	
Daily	0 (0.0)	3 (1.6)	
Triggers of the crisis Malaria, n (%)	28 (66.7)	150 (79.8)	0.102
Hyperthermia, n (%)	5 (11.9)	19 (10.1)	0.780
Physical efforts, n (%)	6 (14.3)	32 (17.0)	0.840
Digestive disorders, n (%)	1 (2.4)	12 (6.4)	0.477

Table 3. Frequency of chronic complications.

Variables	Fréquency (n = 199)%	
Hémolytics		
Gallstones, n (%)	**22**	**11.1**
HTAP, n (%)	12	6.0
Malleolar ulcers, n (%)	21	10.5
Ischémics		
Stroke, n (%)	7	3.5
Ostéonécrosis, n (%)	**33**	**16.6**
Priapism, n (%)	9	4.5
Rétinopathy, n (%)	1	0.5
Infectious		

Continued

Renal failure, n (%)	6	3.0
Septic arthritis, n (%)	23	11.6
Ostéomyélitis, n (%)	**65**	**32.7**

Table 4. Profile of biological examinations carried out according to chronic complications.

Variables	No complications (n = 42)	complications (n = 188)	p-value
Hémoglobin, n (%)	**36 (85.7)**	68 (36.2)	**<0.001**
Thick drop, n (%)	24 (57.1)	101 (53.7)	0.817
Complete blood count, n (%)	**25 (59.5)**	57 (30.3)	**0.001**
VS, n (%)	11 (26.2)	80 (42.6)	0.074
Biochemistry, n (%)	2 (4.8)	19 (10.1)	0.382

Table 5 shows that there is no significant difference regarding monitoring outside of attacks in patients with or without chronic complications.

Table 6 shows that there is a significant association (p = 0.014) between taking analgesics and the presence of chronic complications in 29 (15.4%) sickle cell patients.

4. Discussion

It has been observed that the main factors of chronic complications are belonging to the middle class, the presence of more than one sickle cell patient in the family, the weekly rhythm of crises, the history of transfusion during the last six months preceding the study, lack of monitoring outside of crises and alcohol consumption.

The prevalence of chronic complications in this study was much higher than that found in a study carried out in Cameroon (46.5%) which included 71 homozygous sickle cell patients with a mean age of 24.01 (range: 15 - 58) years [11] In Senegal, Congo and the USA the prevalences of 34.9%, 55.7% and 48% were reported respectively, values lower than those of our study. It should, however, be noted that there is a large variation in the selection of subjects with sickle cell disease and this makes the comparison of different studies that address the problem of chronic complications quite complex.

In our study, osteomyelitis, as a chronic infectious type complication, was the most dominant. Susceptibility to infections, in an unsanitary environment reinforced by precarious living conditions, supports the occurrence of infectious-type complications.

In several studies, hemolytic disorders are the most dominant chronic complications with cholelithiasis as the most frequent hemolytic pathology [11].

Table 5. Profile monitored outside of crises based on chronic complications.

Variables	No complications (n = 42)	complications (n = 188)	p-value
Non crisis monitoring n (%)			0.415
No	7 (16.7)	45 (23.9)	
yes	35 (83.3)	143 (76.1)	
Monitoring frequency, n (%)			0.851
Every month	22 (52.4)	73 (38.9)	
Every 3 months	6 (14.3)	39 (20.7)	
Every 6 months	6 (14.3)	28 (14.9)	
Once a year	1 (2.4)	3 (1.6)	

Table 6. Therapeutic profile outside of crises depending on chronic complications.

Variables	N complications (n = 42)	complications (n = 188)	p-value
Analgesics, n (%)	2 (4.8)	**29 (15.4)**	**0.014**
Antianémics, n (%)	21 (50.0)	68 (36.2)	0.137
Antibiotics, n (%)	13 (31.0)	73 (38.8)	0.437
Anti-inflammatories, n (%)	20 (47.6)	66 (35.1)	0.181
Antioxidants, n (%)	12 (28.6)	35 (18.6)	0.217
Hydroxyurea, n (%)	19 (45.2)	81 (43.1)	0.519

On the other hand, in our study, osteonecrosis was the most frequent ischemic complication, which could be due, in our context, to the fact that not only is its clinical manifestation late but also to the lack of routine monitoring, which remains, is borne by the pocket of the patient or his family.

Cholelithiasis was the most common hemolytic complication. Which is close to the study by Dokekias E. and Nzingoula S. [12]

Among the sociodemographic factors, profession, level of study, socioeconomic level (social class), and belonging to a large family, sometimes with more than one sickle cell patient in the family could be identified as potential factors for the occurrence of chronic complications of sickle cell disease.

The lack of employment (or unemployment) of sickle cell patients from middle socio-economic class families is a combination of factors that are associated with the occurrence of chronic complications due to the lack of sufficient financial and material resources capable of covering medical care, travel costs to get to the hospital or even medications to buy. [13].

The lack of political support for the application of universal health coverage by the State in the holistic care of sickle cell patients requires them to cover all costs linked to the disease. A pilot study carried out at the Center for Mixed Medicine and SS anemia in 2009 estimated the cost of annual treatment for

sickle cell disease at around $1200 - 1500 per child for an average of 6 crises per year [9]. Hence the a need to subsidize the management of sickle cell disease by the state or pooling.

The result found in this work is contradictory to that of Cameroon where patients who had an average socio-economic level had less risk of developing chronic complications. This can be explained by the fact that they may be able to more easily access healthcare or the health policy implemented in their country.

The vicious circle is therefore perpetuated, raising awareness among education personnel of the need to deal with academic difficulties early and to overcome absenteeism secondary to this pathology, by establishing, for example, personalized catch-up lessons with individualized support. by teachers as soon as the child is absent, could therefore ultimately improve the health of sickle cell patients in adulthood. This is the case of the school in a hospital environment, Ecole du cœur within the Ngaliema Clinics in Kinshasa and at CMMASS, a good experience, but unfortunately short-lived due to the lack of a financial support partner to motivate the volunteer teaching staff...

The presence of a brother or sister with sickle cell disease in the family is associated with the risk of developing chronic complications in the sickle cell patient. This situation can create a certain rivalry tinged with intra-fraternal aggressiveness on the part of able-bodied brothers and sisters away from the gaze of the parents. Especially in economically weak families. Members of the siblings of the child or children who are victims of sickle cell disease can abuse the latter, on a psychological level, by insulting them, by belittling them, which can be exacerbated depending on the number of children with sickle cell disease in the community family.

The incidental discovery of the disease is associated with the risk of occurrence of chronic complications of sickle cell anemia. This is in agreement with the work of Diop S. et al. carried out in Senegal [14]. Sickle cell disease still remains little known and ignored by the Congolese population in general, and is most often compared to witchcraft; which diverts patients from the hospital, often sending them to quacks instead of health professionals for proper management of the disease and avoiding possible complications. The delay in diagnosis clearly falls into the context of so-called "orphan" diseases whose development takes more or less five years before an etiological diagnosis can be linked to the pathology [14].

We also observed that the monthly rate of occurrence of attacks as well as the use of analgesics to manage and/or prevent painful attacks are factors associated with chronic complications in our patients. Poorly controlled pain can lead to misuse of analgesic medications; hence, there is also the problem of opiate addiction. The latter can be the cause of multiple conflicts, particularly with the healthcare team. [15]

During the multivariate analysis, the main variables that were significantly associated with the occurrence of chronic complications of sickle cell disease were the following: the average socio-economic level, the presence of more than

one sickle cell patient in the family, the weekly frequency of occurrence of sickle cell seizures, history of transfusion during the last six months preceding the study, lack of follow-up outside of seizures and alcohol consumption.

Patients with sickle cell disease can develop life-threatening complications as well as significant organ damage, reducing both their quality of life as well as their life expectancy [16].

Like any human work, our study presents some limitations which did not allow us to deepen our research.

Our study has the advantage of being one of the first in the Democratic Republic of Congo to address this issue of the impact of factors associated with chronic complications on the quality of life of subjects with sickle cell disease.

In view of these limitations, it would be desirable to provide additional elements to better support and identify other factors associated with the risk of occurrence of chronic complications of sickle cell disease, in order to be able to act on them and circumvent the high risk of morbidity and mortality to which they expose adults with sickle cell disease.

5. Conclusion

The quality of life of sickle cell patients in Kinshasa still remains low overall and particularly in its physical component, significantly affected by psychological limitation.

Improving the living conditions of sickle cell patients for better accessibility to health care services and better monitoring, in particular, the carrying out of the systematic neonatal screening and free subsequent treatment of sickle cell disease should contribute to improving the quality of life of sickle cell patients.

In view of the results obtained, we suggest that for greater objectivity a subsequent study takes into account the clinical and biological elements included in the physical file of the patients who have agreed to participate voluntarily in the study with the possibility of carrying out the control. Of electrophoretic status compared to verbal statements.

Conflicts of Interest

The authors declare no conflicts of interest.

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