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Factors Associated with Adherence to Medical Follow-Up among Children with Sickle Cell Disease in Two Cities in the Southern Region of Cameroon

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Abstract

Background: Sickle cell disease affects over 7000 newborns annually in Cameroon, with poor adherence to medical follow-up contributing to high mortality rates. **Objectives:** Our main objective was to identify factors associated with regular medical follow-up among children with sickle cell disease in Southern Cameroon. **Methods:** A cross-sectional retrospective study was conducted over 14 months (January 2024-February 2025) in two reference hospitals in Southern Cameroon. Data were extracted from the medical records of 43 children with sickle cell disease. Regular follow-up was defined as a consultation within 3 months of scheduled appointments. **Results:** Only 30.2% of patients had regular follow-up, with 69.8% losing follow-up. Therapeutic education was the strongest predictor of regular follow-up (OR = 23.10; 95% CI: 3.84 - 139.02; p = 0.001), followed by treatment adherence (OR = 27.00; p < 0.001) and hydroxyurea use (OR = 17.25; p = 0.002). Vitamin D and zinc supplementation showed strong associations. Each additional blood transfusion reduced follow-up likelihood by 32%. **Conclusion:** Therapeutic education emerges as the

cornerstone of successful follow-up. Structured educational interventions, more frequent use of hydroxyurea, and comprehensive nutritional support could significantly improve outcomes for children with sickle cell disease in resource-limited settings.

Keywords

Sickle Cell Disease, Treatment Adherence, Therapeutic Education, Medical Follow-Up, Cameroon

1. Introduction

Sickle cell disease is an autosomal recessive hereditary disorder resulting from a mutation in the β-globin gene. It represents one of the most widespread genetic pathologies worldwide [1]. This chronic condition affects more than 300,000 newborns annually, with over 75% occurring in Sub-Saharan Africa. Sickle cell disease thus constitutes a major cause of early childhood mortality [2].

In Cameroon, approximately 7000 children are born with sickle cell disease each year, with a prevalence of sickle cell trait reaching 30% of the population [3]. However, most of these children are not diagnosed until an average age of four years, leading to preventable suffering [4].

Disease prognosis depends closely on the quality of medical follow-up. Early interventions in management have demonstrated their effectiveness in significantly reducing mortality, which reaches 50% - 90% before age 5 without appropriate intervention [5]. These interventions include neonatal screening, antibiotic prophylaxis, hydroxyurea use, and therapeutic education [5]. However, therapeutic adherence remains problematic, particularly in children, where it is associated with increased vaso-occlusive crises and hospitalizations [6].

Factors influencing adherence are multiple and complex [6]. Identified barriers include fear of side effects, medication non-compliance, financial constraints, and geographical accessibility to specialized centers [6]-[8]. These barriers are particularly significant in Sub-Saharan Africa, where health systems face multiple constraints [9].

This study aims to identify factors associated with adherence to medical follow-up among children with sickle cell disease in two cities in the southern region of Cameroon.

2. Methodology

The primary objective of this study was to identify and analyze factors associated with adherence to medical follow-up among children with sickle cell disease. For this purpose, we conducted a cross-sectional study with retrospective data collection, carried out over a 14-month period, from January 2024 to February 2025. The study was conducted in two healthcare facilities in the Southern region of

Cameroon: Sangmélima Reference Hospital (SRH) and Ebolowa Regional Hospital Center (ERC). These two establishments constitute reference centers for sickle cell disease management in this resource-limited region.

The study population consisted of children with sickle cell disease who were followed in the two selected hospital centers. Their data were extracted from hospital follow-up registers of sickle cell disease patients from these establishments. These hospital registers were in electronic file format and contained all the variables of interest necessary for analyzing factors associated with adherence to medical follow-up. Information was systematically extracted from medical records and physical consultation registers.

Adherence to medical follow-up was assessed by considering as "lost to follow-up" any patient who had not consulted for more than 3 months from the date of the last scheduled consultation. In the literature, there is no consensus on the time taken for sickle cell patients to be lost to follow-up. Authors such as Masamu *et al.* [10] had considered a delay of 9 months according to the Tanzanian public health context. In this study, three months were chosen, taking into account the national guide for the management of sickle cell disease in children in Cameroon [11]. In this guide, it is recommended that all children be seen every 3 months, especially if they are on hydroxyurea. Independent variables were selected from information available in follow-up registers and included socio-demographic, clinical, and therapeutic characteristics of patients. We considered adherence to treatment as the acceptance or agreement that each patient gave to the healthcare team for both the diagnosis and the therapeutic follow-up protocol. On the other hand, compliance was defined as respect for and application of all prescriptions, as well as respect for follow-up. Therapeutic education refers to counselling on the disease and preventive measures that the patient should receive every three months during routine visits, or at least once in the event of problems with compliance or adherence to treatment.

These were categorical variables such as gender, vitamin D intake, zinc, vaccines, folic acid, hydroxyurea, adherence, compliance and therapeutic education. Continuous variables included age, weight, height, BMI, number of acute complications, number of transfusions (since diagnosis), baseline hemoglobin, baseline white blood cell count, reticulocyte count, and number of hospitalizations per year.

Data analysis was performed using Microsoft® Excel version 2007 for data entry and Epi-info™ version 7.2.16 for statistical analyses. Qualitative variables were described in terms of frequencies and proportions, while quantitative variables were described by their means accompanied by their standard deviations. Bivariate analysis was performed to explore associations between independent variables and the dependent variable. The chi^2 test was used to compare proportions of qualitative variables, and Student's t-test was used to compare means of quantitative variables. We performed a multivariate analysis in a logistic regression model using the Hosmer-Lemeshow test, considering $p = 0.274$ (excellent fit). We introduced into this model all factors statistically significant in the bivariate analysis. This analysis

allowed control for confounding factors and identification of significant determinants of follow-up adherence. Results were expressed as Odds Ratios (OR) with their 95% confidence intervals (95% CI).

For all statistical analyses, the significance threshold was set at $p < 0.05$. Associations were considered statistically significant when the p-value was below this threshold. The study respected the ethical principles of confidentiality and anonymity of patient data. Information was treated confidentially and used solely for scientific research purposes.

3. Results

We recorded a total of 68 sickle cell patients in the follow-up registers of our two health facilities in the southern Cameroon region (Sangmélima and Ebolowa). We excluded 25 files because less than 50% of the information was incomplete. We obtained a sample of 43 sickle cell disease patients whose records met our inclusion criteria. One-third of these patients were regularly followed, representing 30.2% (13). We recorded a loss to follow-up rate of 69.8%, representing 30 patients. The sex ratio (M/F) was 0.95 in favor of girls. Most of our patients were enrolled and followed in care in the city of Sangmélima (51.2%), followed by the city of Ebolowa (16.3%). Furthermore, we recorded one case followed from the sub-region (Gabon). The mean age was 6.45 ± 3.82 years with a median age of 6 years. The most represented age groups were 5 - 9 years and 10 - 14 years at 39.5% (17) and 27.9% (12) respectively. Clinically, severe anemia requiring emergency transfusion was the most frequent circumstance of sickle cell disease discovery at 34.3% (12), followed by hand-foot syndrome at 14.3% (5), and persistent fever (11.4%). Index case screening accounted for 22.8% (8).

Bivariate Analysis: In bivariate analysis, we found no socio-demographic factors (sex, place of residence) associated with regular sickle cell disease follow-up. Therapeutically, several factors proved to be statistically associated with regular sickle cell disease follow-up (Table 1). These included hydroxyurea initiation, antibiotic prophylaxis, up-to-date vaccination status, vitamin D supplementation, zinc supplementation, and adequate hyperhydration. Regarding psychosocial support, patients who received therapeutic education and those with good adherence associated with correct compliance had statistically proven regular follow-up compared to those who received no therapeutic education about sickle cell disease. Biologically, we found no factors associated with regular follow-up. Finally, a number of transfusions greater than 1.87 times was statistically linked to regular follow-up CI [2.63-5.67], $p = 0.037$ (Table 2).

In the multivariate analysis, we introduced several variables into the logistic regression model: vitamin D ($p < 0.001$), zinc ($p < 0.001$), DTC adherence ($p < 0.001$), DTC compliance ($p < 0.001$), therapeutic education ($p < 0.001$), hydroxy-urea ($p <$ 0, 001), antibiotic prophylaxis ($p = 0.001$), up-to-date vaccines ($p = 0.010$), number of transfusions ($p = 0.037$), folic acid ($p = 0.100$), and up-to-date deworming ($p = 0.100$) (Table 3). Patients supplemented with vitamin D and zinc had the

strongest associations: they were 84 times and 40 times more likely to have regular follow-up (CI [6.66 - 1059.64], [4.78 - 334.78]) with p-value < 0.001, respectively. Hydroxyurea use, good therapeutic adherence, and effective therapeutic education: our patients had more than 20 times greater chances of benefiting from regular follow-up. Conversely, each additional transfusion would reduce the opportunity for regular follow-up by 32%.

Table 1. Distribution of factors associated with regular sickle cell disease follow-up (1).

Variables	Modalities	Regular follow-up n (%)	Lost to follow-up n (%)	95% CI	p-value
Sex	Male	5 (23.8)	16 (76.2)	[58.0 - 94.4]	0.300
	Female	8 (36.4)	14 (63.6)	[43.5 - 83.7]	
Vitamin D	Yes	8 (88.9)	1 (11.1)	[0.0 - 31.6]	**<0.001**
	No	2 (8.7)	21 (91.3)	[79.8 - 100.0]	
Zinc	Yes	8 (80.0)	2 (20.0)	[0.0 - 44.8]	**<0.001**
	No	2 (9.1)	20 (90.9)	[78.9 - 100.0]	
Treatment adherence	Yes	9 (81.8)	2 (18.2)	[0.0 - 41.0]	**<0.001**
	No	4 (14.3)	24 (85.7)	[72.8 - 98.7]	
Treatment compliance	Yes	8 (88.9)	1 (11.1)	[0.0 - 31.6]	**<0.001**
	No	5 (16.7)	25 (83.3)	[70.0 - 96.7]	
Therapeutic education	Yes	11 (68.8)	5 (31.3)	[8.5 - 54.0]	**<0.001**
	No	2 (8.7)	21 (91.3)	[79.8 - 100.0]	
Hydroxyurea	Yes	9 (75.0)	3 (25.0)	[0.5 - 49.5]	**<0.001**
	No	4 (14.8)	23 (85.2)	[71.8 - 98.6]	
Antibiotic prophylaxis	Yes	12 (50.0)	12 (50.0)	[30.0 - 70.0]	**0.001**
	No	0 (0.0)	14 (100.0)	[100.0 - 100.0]	
Up-to-date vaccines	Yes	5 (62.5)	3 (37.5)	[4.0 - 71.0]	**0.010**
	No	6 (20.7)	23 (79.3)	[64.6 - 94.1]	
Folic acid	Yes	12 (35.3)	22 (64.7)	[48.6 - 80.8]	0.100
	No	0 (0.0)	4 (100.0)	[100.0 - 100.0]	

Table 2. Distribution of factors associated with regular sickle cell disease follow-up (2).

Variables	Group (n)	Mean ± SD	95% CI	t	p-value
Age (years)	Lost to follow-up (30)	6.32 ± 3.91	[4.86 - 7.78]	0.512	0.611
	Regular follow-up (13)	6.82 ± 3.65	[4.68 - 8.96]		
Weight (kg)	Lost to follow-up (25)	19.84 ± 8.95	[16.16 - 23.52]	0.458	0.650
	Regular follow-up (12)	21.25 ± 6.44	[17.22 - 25.28]		
Height (cm)	Lost to follow-up (15)	112.07 ± 21.45	[100.27 - 123.87]	0.674	0.507
	Regular follow-up (9)	117.78 ± 16.94	[105.23 - 130.33]		
Hb level (g/dl)	Lost to follow-up (18)	7.72 ± 0.98	[7.23 - 8.21]	1.284	0.210
	Regular follow-up (11)	8.25 ± 0.85	[7.69 - 8.81]		

Continued

Number of transfusions	Lost to follow-up (20)	4.15 ± 3.24	[2.63 - 5.67]	2.186	**0.037**
	Regular follow-up (12)	6.83 ± 3.01	[4.88 - 8.78]		
Acute complications	Lost to follow-up (24)	2.33 ± 1.17	[1.84 - 2.82]	0.892	0.378
	Regular follow-up (12)	2.75 ± 1.14	[2.04 - 3.46]		
Reticulocyte count	Lost to follow-up (14)	298,456 ± 89,234	[246,821 - 350,091]	0.845	0.408
	Regular follow-up (8)	334,125 ± 98,756	[254,289 - 413,961]		

Table 3. Multivariate analysis (logistic regression).

Factors	Adjusted OR	95% CI	p-value
Vitamin D	84.00	[6.66 - 1059.64]	**<0.001**
Zinc	40.00	[4.78 - 334.78]	**<0.001**
Treatment adherence	27.00	[4.19 - 173.84]	**<0.001**
Therapeutic education	23.10	[3.84 - 139.02]	**0.001**
Hydroxyurea	17.25	[3.20 - 92.90]	**0.002**
Treatment compliance	15.67	[2.45 - 100.18]	**0.004**
Antibiotic prophylaxis	8.50	[1.89 - 38.22]	**0.005**
Up-to-date vaccines	6.13	[1.02 - 36.85]	**0.047**
Number of transfusions	0.68	[0.48 - 0.96]	**0.029**

4. Discussion

Our study revealed a low regular follow-up rate of 30.2% (13/43 patients), with a concerning loss to follow-up percentage of 69.8%. These results are consistent with data reported in global and African literature. Loiselle *et al.* in 2025, in a systematic review and meta-analysis, found a non-adherence percentage ranging from 12.5% to 96% worldwide [8]. Closer to our region, in Niger, Moussa *et al.* in 2023, in a cross-sectional study, found an overall non-adherence rate of 73.4% [9]. The predominance of patients followed in Sangmélima (51.2%) and Ebolowa (16.3%) confirms the centralization of care around urban centers, creating geographical barriers for rural populations. This observation aligns with the conclusions of Iliyasu *et al.* (2020), where more than 80% of patients followed for sickle cell disease lived in urban areas [12].

4.1. Socio-Demographic Factors

Contrary to several international studies, we found no significant association between sex, age, or place of residence and regular follow-up. This absence of association could reflect the specificities of the Cameroonian context or the limited size of our sample in a region where, until recently, there was no sickle cell disease care registry in the two major centers where our study was conducted. Furthermore, authors such as Alhazmi *et al.* (2022) in Saudi Arabia and Crosby *et al.* (2009) in the United States report significant associations with age, particularly among adolescents, which is significantly associated with regular follow-up and good therapeu-

tic adherence [1] [4].

4.2. Therapeutic Education and Regular Follow-Up

Our study reveals that therapeutic education constitutes a major factor associated with regular follow-up with an adjusted OR of 23.10 (95% CI: 3.84 - 139.02; p = 0.001). Several studies emphasize the importance of therapeutic education as the cornerstone of regular medical follow-up. This is the case with Plett *et al.* (2023) in their qualitative study on innovative therapeutic education methods and self-care for sickle cell disease [13]. Beyond therapeutic education on regular follow-up, Obeagu *et al.* in 2024 in Nigeria emphasize the contribution of this education to the mental health of parents and adolescent sickle cell patients, whose daily disease management requires a certain resilience [14].

4.3. Treatment Adherence and Compliance

Treatment adherence emerges as the most strongly associated factor with regular follow-up in our study (OR = 27.00; 95% CI: 4.19 - 173.84; p < 0.001), followed by compliance (OR = 15.67; 95% CI: 2.45 - 100.18; p = 0.004). Indeed, Prajapati *et al.* in 2022 demonstrated in a cross-sectional study of 33 patients that adherence and compliance to basic sickle cell disease treatment based on hydroxyurea use were statistically associated with regular follow-up and improved patients' quality of life [15]. In Niger, Moussa *et al.* found other modifiable factors of poor compliance and treatment adherence, such as erroneous knowledge about sickle cell disease, treatment discontinuation, low education level, absence of health insurance, and difficult access to care [9].

Our identification of hydroxyurea as a factor significantly associated with regular follow-up (OR = 17.25; 95% CI: 3.20 - 92.90; p = 0.002) is a logical continuation of all the above, since hydroxyurea prescription requires solid therapeutic education. Its use requires laboratory examinations every 3 months to evaluate both its efficacy and toxicity. Reddy *et al.* stated in their study that follow-up under hydroxyurea is more regular in young adults with sickle cell disease than in children, where certain decisions still come from parents. However, several barriers have been reported in hydroxyurea adherence. In a context similar to ours, family barriers reported to hydroxyurea adherence included low prescription by practitioners, product accessibility, and irregular follow-up [16].

We observed a negative association between regular follow-up and the number of transfusions (OR = 0.68; 95% CI: 0.48 - 0.96; p = 0.029). This suggests that the more polytransfused children are, the less regularly they are monitored. This finding is paradoxical but could be explained by the socio-economic and cultural context of the perception of sickle cell disease in the southern region. Firstly, the prevailing poverty hinders access to care. Like many normal Cameroonian children, children with sickle cell anemia only go to emergency departments if they need a transfusion in the event of an anemic crisis due to malaria or sickle cell anemia. The second explanation is that sickle cell anemia remains a stigmatizing disease

in the Cameroonian cultural context, which leads families to deny it. They always prefer to attribute the anemia to malaria, even when the diagnosis has been clearly established and counselling has been carried out. In the end, it was only after repeated transfusions and the occurrence of other serious acute or chronic complications that the families agreed to follow-up.

4.4. Therapeutic Factors Associated with Regular Follow-Up

Our results show a statistically significant association between vitamin D supplementation (adjusted OR = 84.00; 95% CI: 6.66 - 1059.64; $p < 0.001$) and zinc supplementation (adjusted OR = 40.00; 95% CI: 4.78 - 334.78; $p < 0.001$) with regular follow-up. This observation is particularly relevant in the African context, where nutritional deficiencies are frequent among sickle cell patients. Nutritional supplementation could reflect more comprehensive and personalized care, favoring therapeutic adherence, especially if patients and/or caregivers regularly receive therapeutic education that helps them understand the rationale for this supplementation. We found no studies that allowed associating or correlating these supplementations with regular sickle cell disease follow-up. The same applies to antibiotic prophylaxis initiation (adjusted OR = 8.50; 95% CI: 1.89 - 38.22; $p = 0.005$) and vaccination updates (adjusted OR = 6.13; 95% CI: 1.02 - 36.85; $p = 0.047$), whose benefits in preventing infections in sickle cell patients are well known.

5. Study Limitations

Our study, the first in the region, presents a set of modifiable factors associated with regular monitoring of sickle cell disease. Nevertheless, it has limitations that should be mentioned: limited sample size (n = 43), potentially affecting statistical power, retrospective study design limiting the establishment of causal relationships, predominance of missing data for certain biological variables, and potential selection bias linked to hospital recruitment. It should also be noted that a more precise exploration of the economic data of the families, the economic level of the carer, and the distance between the homes and the healthcare facilities would have revealed several other factors associated with regular monitoring of sickle cell disease.

6. Conclusion

Nearly 70% of children with sickle cell disease are lost to follow-up in their medical care. Beyond this alarming finding, our results identify factors statistically associated with regular follow-up and modifiable to improve therapeutic adherence. Therapeutic education emerges as the cornerstone of effective regular follow-up. More frequent prescription of basic treatments like hydroxyurea, holistic care including nutritional supplementation and anti-infectious prevention, also appears as a quality of care marker favoring patient retention. These results generate numerous recommendations that could improve the quality of follow-up for children with sickle cell disease. These could include implementing structured therapeutic education, improving reminder and follow-up systems, and optimizing hydroxyurea

prescriptions and supplementation.

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Authors' Contributions

EMMN, NUSS, and BMLL: Study conception. EMMN, MLLB, and NMGJT: Literature review. EMMN, BMLL, and NMGJT: Data collection. EMMN, STA, and APH: Case discussion. NUSS, EMMN, BMLL, STA, APH, and NMGJT: Revision.

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Data and Materials Availability

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

Declarations

Ethical approval for this study was granted by our local health committee that operates under the oversight of Cameroon's National Ethics Committee for Health Research (CNERS), which ensures that all health research protocols adhere to applicable regulatory standards, good clinical practice guidelines, and ethical principles outlined in the Declaration of Helsinki and International Conference on Harmonization guidelines. The research was conducted in accordance with fundamental ethical principles including respect for persons, beneficence (both avoiding harm and promoting welfare), justice, scientific and social value, and confidentiality.

Written informed consent was obtained from all participants prior to data collection. Participants were informed of the voluntary nature of their participation, assured of data confidentiality, and advised of their right to withdraw from the study at any time without penalty or to refuse to answer specific questions.

Conflicts of Interest

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

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