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Hemoglobin phenotypes of children attending pediatric clinics in Lomé, Togo, 2022

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Abstract

Objective To provide an up-to-date data, we aim to estimate the frequency of sickle cell disease among children in the pediatric clinics of the Sylvanus Olympio University Hospital, Lome, Togo, in 2022.

Results A total of 317 children with a median age of 8 years (Interquartile range: 4–12) were included. Both parents knew their Hb phenotype in 7.3% of cases. Nineteen children had sickle cell disease (6.0%) and about 15.6% of the children had sickle cell trait AS. This study found a high frequency of children with sickle cell disease seen in pediatric clinics. We therefore emphasize the need for continued education to improve knowledge of the hemoglobin phenotype at community level and the importance of premarital screening to reduce this burden in the country.

Keywords Sickle cell disease, Children, Hospital frequency, Togo

Background

Every year, over 200,000 children are born with sickle cell disease (SCD) in Africa. Worldwide, the number of healthy carriers (having inherited a mutant gene from one parent) in certain regions leads to a high rate of newborns affected by this condition [1]. Because of the significant health, social and economic impact of the disease, it is a major public health concern.

Early detection is one of the fundamental pillars in the fight against SCD and helps to extend the life expectancy of patients. According to the 2020's World Health Organization (WHO) Afro report on progress in implementing the SCD strategy, early detection remains insufficient. Indeed, only twelve out of forty-seven Member States carry out early screening for SCD at sub-national level [2].

Sickle cell disease is a group of inherited blood disorders that results in the production of unusual hemoglobin (Hb) or Hb variant. There are several types of SCD, some more severe than others. The genes a person inherits from their parents determine the specific type of SCD. Hemoglobin SS, SC, and S beta thalassemia phenotypes are the most commonly described. People who have Hb SS, sickle cell anemia (SCA), inherit two genes, one from each parent, that code for hemoglobin "S". In the other two forms, people inherit not only the gene that codes for hemoglobin S, but also a second gene that codes for another Hb variant such as, hemoglobin C, D,

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E, G or beta thalassemia [3]. In someone who has SCD, hemoglobin is unusual, and causes the red blood cells to become rigid (poorly deformable) and sticky and look like a C-shaped farm tool called, 'a sickle'. The sickle cells have a short life span, which causes a constant shortage of red blood cells. Also, as they pass through small blood vessels, sickle cells stick to the blood vessels and to each other and clog the blood flow. This may cause painful crises and other serious complications (health problems) such as infection, acute chest syndrome, and stroke [3]. Sickle cell trait (SCT) is a sickle cell disorder (Hb AS), which usually does not cause any signs of the disease. However, in rare cases, an individual with SCT may have pain or any other symptom associated with SCD when subjected to stressful conditions, e.g. hypoxia, dehydration or strenuous exercise [3].

In a study published in 2002 in Togo on 5604 samples, the main unsual hemoglobins were the S (AS trait 15.8 to 16.7%) and C (AC trait 12.1 to 15.8%) variants [4]. Sickle cell anemia was observed in 1.2 to 2% of subjects and sickle cell SC disease in 4.2% [4]. The national health development program for the years 2017 to 2022, prioritized the fight against non-communicable diseases including SCD in the health policy and control component [5].

Togo, like most countries in the WHO Afro Region, lacks accurate and reliable data on the frequency of SCD. In addition, data collection on SCD is hardly included in most national population surveys, such as STEPS (WHO recommended tool for monitoring risk factors for non-communicable diseases) and DHS (Demographic and Health Survey) [6]. Furthermore, financial and geographical inaccessibility in southern countries make it difficult to access screening for the disease.

To bridge this screening gap, and since hospital-based studies may provide a means of recourse [7], we therefore, aimed to determine the frequency of SCD among children attending pediatric clinics in a tertiary hospital in Lome, Togo.

Methods

Design and study population

This was a sub-study of a cross-sectional survey whose primary objective was to estimate the hospital seroprevalence of SARS-CoV-2 among children by HIV serostatus. The study was conducted from August to November 2022 in the pediatric clinics of the Centre Hospitalier Universitaire Sylvanus Olympio (CHU-SO) in Lomé, Togo. The hospital is a tertiary care facility, which serves as a reference center for the Greater Lomé health region. This study was approved by the Bioethics Committee for Health Research of the Ministry of Health (N°002/2021/CBRS). We present here a secondary analysis, which focuses on estimating the frequence of SCD among children in the pediatric clinics of the Sylvanus Olympio University Hospital, Lome, Togo, in 2022.

All children attending the study site were invited to participate and included if: (i) aged between 18 months and 19 years, (ii) present in pediatric clinics and (iii) provided assent and/or parental informed consent.

Data collection

Data were collected using a digital questionnaire through a face-to-face interview. The collection tool was structured into five sections: (i) sociodemographic characteristics, (ii) clinical characteristics (iii) parents' self-reported hemoglobin phenotype, (iv) children's hemoglobin phenotype.

Biological samples and tests

A venous blood sample of 4–5 ml was taken from all the participants under aseptic conditions. Samples were stored on site and transported to the laboratory within 5 h for hemoglobin electrophoresis on a cellulose acetate plate at alkaline pH, using the Helena electrophoresis chain (*Model N° 1501 Serial N° 2186 Beaumon Texas USA/ Cuve de migration HELENA LABORATOIRES Model N° 1283 Serial N° 9361 Beaumon Texas USA / Etuve Incubator Oven Dryer HELENA Laboratoires Model N°51/7 220 Serial N° IOD 15/80 Beaumon Texas US / Scanner Epson J221A Seiko Epson Corp. Japan Model N° J221A Serial N° G33W025539*) [8]. Sickle cell disease was defined as having either hemoglobin SS, SC, SF, or Sß phenotype.

Statistical analysis

Categorical and quantitative variables were presented as numbers with their proportions and median with their interquartile range (IQR), respectively. The frequency and 95% confidence interval (95% CI) of the SCD phenotypes were estimated. Categorical variables were compared using chi-square tests or Fisher's exact test, and quantitative variables were compared using the non-parametric Wilcoxon test. The significance level was set at 5%. R-studio version 4.2.0 (The R Foundation for Statistical Computing Platform) was used for all statistical analyses.

Case management

Results were available within 7 days of inclusion from a pediatrician. All participants received counseling on the disease and its transmission, whatever their result. Participants who were found to have SCD were referred to the *Centre National De Recherche et de Soins aux Drepanocytaires* (CNRDS), the SCD reference center in Togo.

Results

Socio-demographic characteristics

A total of 317 children with a median age of 8 years (IQR: 4–12) were included. Approximately 44.5% ($n = 138$) of the children were female. The majority were outpatients (63.9%) and 48.3% ($n = 152$) had reached primary school level. In 81.4% of the patients, the parents did not know their haemoglobin phenotype. Details of socio-demographic data are summarized in Table 1.

Table 1 Sociodemographic characteristics of children and parent's hemoglobin phenotypes

Variable	Sex			
	Female $N = 138$[1]	Male $N = 179$[1]	Overall $N = 317$[1]	*p*-value[2]
Age (yr), Median (IQR)	8 (4–12)	7 (4–11)	8 (4–12)	0.469
Age classes (yr)				0.389
< 5	41 (29.7)	47 (26.3)	88 (27.8)	
5–9	39 (28.3)	67 (37.4)	106 (33.4)	
10–14	39 (28.3)	45 (25.1)	84 (26.5)	
15–19	19 (13.7)	20 (11.2)	39 (12.3)	
Type of patient				0.981
Outpatient	87 (64.0)	113 (63.8)	200 (63.9)	
Hospitalized	49 (36.0)	64 (36.2)	113 (36.1)	
Missing data	2	2	4	
Level of Education of children				0.252
No formal education	38 (27.9)	43 (24.0)	81 (25.7)	
Primary	57 (41.9)	95 (53.1)	152 (48.3)	
Secondary	32 (23.5)	33 (18.4)	65 (20.6)	
Tertiary	9 (6.6)	8 (4.5)	17 (5.4)	
Missing data	2	0	2	
Father's hemoglobin phenotype				0.215
AA	9 (6.6)	15 (8.4)	24 (7.6)	
AC	0 (0.0)	2 (1.1)	2 (0.6)	
AS	2 (1.4)	8 (4.5)	10 (3.2)	
Unknown	126 (91.3)	154 (86.0)	280 (88.3)	
SBThal	1 (0.7)	0 (0.0)	1 (0.3)	
Mother's hemoglobin phenotype				0.079
AA	9 (6.5)	18 (10.0)	27 (8.5)	
AC	1 (0.7)	1 (0.6)	2 (0.6)	
AS	3 (2.2)	13 (7.3)	16 (5.0)	
Unknown	125 (90.6)	147 (82.1)	272 (85.9)	
Parents' knowledge of their hemoglobin status				0.031
None	117 (84.8)	141 (78.8)	258 (81.4)	
One	17 (12.3)	19 (10.6)	36 (11.4)	
Both	4 (2.9)	19 (10.6)	23 (7.2)	

[1]Median (25-75%); n (%)

[2]Wilcoxon-Mann-Whitney test; Fisher's exact test; chi-square test of independence

Distribution of patients according to hemoglobin phenotypes

Of the 317 children screened for phenotyping, 19 had SCD (SS/SC/SF/Sβ phenotype), representing a frequency of 6.0% [95% CI: (3.7–9.4)]. The proportion of SCD was significantly higher in males than in females (8.5% vs. 2.9%, $p = 0.039$). Approximately 15.6% of the children had sickle cell trait AS (Fig. 1).

Parents' hemoglobin phenotype and children SCD frequency

Both parents knew their hemoglobin phenotype in 7.3% (23/317) of cases. The frequency of SCD was 17.4% in children whose parents' knew their hemoglobin phenotype, versus 5.1% in children whose parents did not know their hemoglobin phenotype ($p = 0.074$; Table 2).

Discussion

This was a cross-sectional study, with the aim of determining the hospital frequency of SCD in children attending the pediatric clinics of the CHU SO, Togo in 2022.

Although recent studies have shown considerable variation between countries, the frequency of attendance at hospital clinics and wards for children with SCD in Africa remains poorly documented. In the Democratic Republic of Congo, Aimé et al., (2022), reported an estimated hospital frequency of 31.9% in children under 5 years of age, with a distribution of 12.7% for the homozygous (Hb SS) and 19.2% for the heterozygous phenotypes [9]. Another study conducted at Al Fashir University Hospital, Sudan, found a frequency of 14.8% in children aged under 18 years [9]. The data from our study reported an estimated hospital frequency of 6.0% with a distribution of 2.2% for the homozygous (Hb SS) and 3.8% for SC phenotype. The SC phenotype frequency is not surprising given that Hb C circulation has been reported in West Africa, most commonly in Mali, Burkina Faso and Ghana [10]. This may also indicate historical patterns of migration and intermarriage among groups in the sub-region, particularly in Togo. In this study, none of our patients were reported to have compound heterozygous Hb Sβ thalassaemia, possibly because the β thalassaemia allele is rare in Togo [11]. Overall, the figures are worrying and could be partly explained by a lack of awareness of the disease among the population.

As found in our study, more than eight in ten parents were unaware of their hemoglobin phenotype, which prevented them from receiving appropriate genetic counseling. Similarly, Mombo et al. in Gabon in 2021, reported that only 6% of pregnant women knew their hemoglobin phenotype [12]. These data first of all reveal the need for more community awareness on SCD to improve knowledge of hemoglobin phenotype and ability to make objective decisions concerning reproduction life among adults

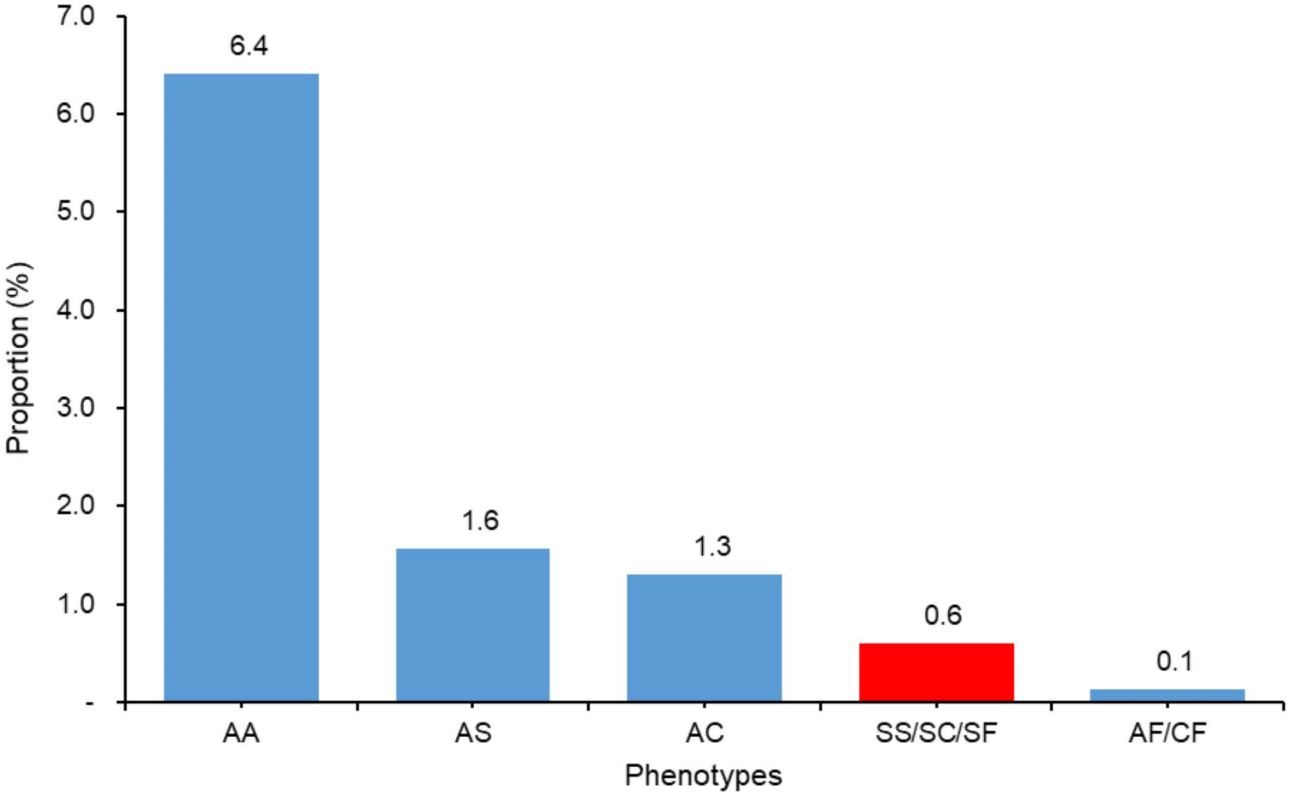

Fig. 1 Frequency of sickle cell phenotypes

Table 2 Frequency of sickle cell disease according to sociodemographic characteristics of children and parent's knowledge of their hemoglobin phenotype

Variable	*N*	*n*	%	95%CI	*p*-value[2]
Age classes (yr)					0.532
< 5	88	5	5.7	2.1–13.4	
5–9	105	4	3.8	1.2–10.0	
10–14	83	7	8.4	3.7–17.1	
15–19	39	3	7.7	2.0–22.0	
Sex					**0.039**
Female	138	4	2.9	0.9–7.7	
Male	177	15	8.5	7.6–20.6	
Parents' knowledge of their hemoglobin phenotype					0.074
None	256	13	5.1	2.8–8.7	
One	36	2	5.6	0.9–20.0	
Both	23	4	17.4	5.7–39.5	

[1]Median (25-75%); n (%)

[2]Fisher's exact test

*Sickle cell disease = SS/SC/SF phenotype

and adolescents. It secondly shows that an update in the population-based data is needed in order to assess the current prevalence of the disease needed to modify policies for the control of the disease [13].

Indeed, genetic counseling is a communication process by which the counselor ensures that clients gain adequate and correct understanding of the genetics of the disease, while remaining sensitive to the emotional state of the client [14]. During counseling, hemoglobinopathy counselors establish and document information of the disease in question in a three-generational pedigree of the client and demonstrates the chances of inheriting SCD. The counselor may then offer the client tests to undergo that would confirmed the hemoglobin type and enable the client to make informed decision [15].

Newborn screening pilot initiatives for hemoglobinopathies were implemented in Angola, Nigeria, Ghana, the Democratic Republic of Congo, and the Republic of Benin [16]. The cost of testing, lack of sufficient and accessible medical records, and inadequacy in healthcare infrastructure pose significant challenges in bridging the gaps in newborn screening [16]. In the absence of neonatal screening, we propose systematic screening of children at immunization centers as an alternative method to facilitate rapid treatment of children with sickle cell disease and to raise awareness among parents. In both these options, the use of accurate point-of-care diagnostic tests that demonstrated high performance even on newborn cord blood [17, 18], should be seriously considered.

Originality and limitations

Our study provides updated data on SCD in Togo, the last study dating back to 2002 [4]. Moreover, the study

is based on data from screening in patients who were unaware of their hemoglobin phenotype. However, the results must be interpreted in the light of the study's limitations. Firstly, this was a hospital survey, and the data cannot be extrapolated to the national level. It then seems urgent to carry out a national study to confirm the trend reported in this study. Secondly, we used alkaline agarose gel electrophoresis, as this was the technique available at the time of the study. Although this method is also capable of separating different forms of hemoglobin, it is less resolutive than high-performance liquid chromatography, or isoelectric focusing (IEF) technique in distinguishing between structurally very similar hemoglobins, which could lead to less accuracy in diagnosing hemoglobin disorders.

Conclusion

This study found a high frequency of SCD in children seen in pediatric clinics. In addition, more than eight out of ten parents were unaware of their hemoglobin phenotype. We therefore emphasize the need for continued education to improve knowledge of the hemoglobin phenotype at community level and the importance of premarital screening and counseling to reduce the prevalence of SCD in the country.

Abbreviations

CHU-SO	Centre Hospitalier Universitaire Sylvanus Olympio
CI	Confidence interval
CNRDS	Centre National De Recherche et de Soins aux Drepanocytaires
Hb	Hemoglobin
IEF	Isoelectric focusing
IQR	Interquartile range
SCD	Sickle cell disease
SCT	Sickle cell trait
WHO	World Health Organization

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Author contributions

YRK and DKE conceived the study, developed the protocol and contributed to the study design. OIWA, KFS and OET collected the data. FAL performed, verified and supervised biological procedures for hemoglobin status detection under the supervision of MK. Statistical analysis was performed by OIWA and YRK. HRK, KHG drafted the manuscript. All the authors reviewed the manuscript.

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Data availability

Data may be obtained from corresponding author upon reasonable demand.

Declarations

Ethics approval and consent to participate

This study was approved by the Bioethics Committee for Health Research of the Ministry of Health (Number 002/2021/CBRS). For participants under 16 years of age, informed consent was obtained from their parents or legal guardians, along with their assent. For participants aged 16 and older, free and informed consent was obtained prior to enrollment.

Consent for publication

Written informed consent for publication was obtained from all of the participants aged 18 and over, as well as the parents or legal guardians of any participant under the age of 18.

Competing interests

The authors declare no competing interests.

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