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Newborn screening for sickle cell disease in Lubumbashi, Democratic Republic of the Congo: An update on the prevalence of the disease

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ABSTRACT

Objectives: Sickle cell disease (SCD) is an autosomal recessive hemoglobinopathy. It affects about 2% of newborns in some sub-Saharan African countries. In most patients, the incidence of complications can be reduced if screening takes place at birth. This study was conducted to determine the prevalence of SCD among a population of newborns in Lubumbashi, in the Democratic Republic of the Congo (DRC).

Material and Methods: This prospective and cross-sectional study was conducted among newborns in five referral maternity hospitals in Lubumbashi city, in the DRC. Newborns' blood samples were examined by capillary electrophoresis.

Results: Of a total of 588 newborns screened for SCD, 369 (68.59%; 95% confidence interval [CI]: 64.48%–72.49%) newborns were Hemoglobin AA (HbAA); 141 (26.21%; 95% CI: 22.54%–30.14%) newborns were HbAS; 27 (5.01%; 95% CI: 3.33%–7.22%) newborns were HbSS, and 1 (0.19%; 95% CI: 0.00%–1.03%) newborn was Hemoglobin AC (HbAC).

Conclusion: The present study determined the prevalence of SCD during neonatal screening in Lubumbashi. The conduct of premarital counseling is essential to reduce the prevalence of this hemoglobinopathy which is high (5.01% of HbSS). Systematic newborn screening in all maternity wards in the country would help to assess the prevalence at the national level and improve the quality of life of SCD children.

Keywords: Sickle cell disease, Neonatal screening, Prevalence, Newborn, Lubumbashi

INTRODUCTION

Sickle cell disease (SCD) is an inherited hemoglobinopathy resulting from the substitution of the amino acid glutamic for valine in the sixth position of the beta-globin chain.[1] The inheritance of the sickle cell trait follows an autosomal recessive pattern. Phenotypically, only individuals with double recessive sickle cell genes Homozygous sickle cell [Hemoglobin SS (HbSS)] manifest disease, while Heterozygotes [Hemoglobin AS (HbAS)] are called carriers.

According to Diallo, Africa is the most affected continent with 200,000 newborns with SCD per year.[2] This represents about 66.6% of children born with hemoglobinopathies worldwide. The lack of reliable data in most countries makes it difficult to estimate the actual number of people affected worldwide. There are no national registries on the disease, even in developed countries

that have had newborn screening programs in place for several years (USA, United Kingdom, France).[3] Various estimates have been published[3-5] reporting highly variable frequencies of S allele distribution according to region: Sub-Saharan Africa (about 20 countries with 2–38%), India (6 regions with 17–30%), Eastern Mediterranean (Saudi Arabia [1–29%], and Iraq [0–22%]). In the Democratic Republic of the Congo (DRC), the latest studies report a prevalence of up to 40% of the population for the heterozygous form among carriers of the sickle cell trait (otherwise known as healthy carriers), and up to 2.3% of the population for the homozygous form among SCD patients. The DRC records about 40,000 births of children with SCD each year.[6] According to reports from Ghana, an estimated 15,000 children are born with SCD each year.[7] In Benin, the prevalence of sickle cell trait is estimated at 25%[8] while in Nigeria, it varies from 24% to 25%.[9,10] In all these African countries, the concentration of the sickle cell trait has been found to be highest in specified subpopulations,[2,9,10] probably due to conservative tribal marriages. The autosomal recessive inheritance pattern assumed by the sickle cell trait, however, predicts changes in population-level dynamics, ease of movement, and intermarriage that would alter the distribution of the sickle cell trait within these communities.[11]

Available data on the prevalence of SCD in a population of newborns in Lubumbashi are based on a preliminary survey conducted by Shongo and Mukuku in 2017.[12] According to this study, the prevalence of sickle cell trait among these newborns was 15.61% (3.47% of newborns were carriers of homozygous sickle cell [HbSS] and 12.14% were heterozygous sickle cell [HbAS]).[12]

In light of advances in health interventions, screening, and premarital counseling of the population, it is assumed that the distribution of the sickle cell trait among African populations can be strategically altered. We hypothesized that a current survey on the prevalence of SCD in Lubumbashi will be informative given that 5 years have already elapsed since the last study which was only preliminary.[12] This study was therefore conducted to establish an update on the prevalence of the sickle cell trait in the city of Lubumbashi, in the DRC.

MATERIAL AND METHODS

Framework and type of study

This was a prospective, cross-sectional, and descriptive study involving newborns. We conducted neonatal screening for SCD in the maternity wards of five health facilities in the city of Lubumbashi, in the DRC, from June to December 2020. These were University Clinics, Jason Sendwe Hospital, Katuba General Referral Hospital, Kamalondo General Hospital, and Kenya General Referral Hospital.

Study population

This study included newborns born in the above maternity units and the screening involved newborns <7 days old. Informed consent was sought from any woman who agreed to have her newborn screened. The study excluded any newborn with any disease diagnosed during their maternity stay, any transfused newborn, and any newborn whose mothers did not agree to participate in the study. Demographic and contact information was collected before blood sample collection using a pre-designed form and was then entered into a database in Microsoft Excel format.

The Cochran formula for descriptive studies was used to calculate the sample size ($n = z^2pq/d^2$),[13] with a 95% confidence interval (CI) standard deviation (1.96), an estimated sickle cell prevalence of 3.47%[12] and a precision error of 2.5% (0.025). The minimum sample size calculated was 206 participants. Taking into account a non-response rate of 20%, a sample size of 248 was calculated, but 538 newborns were finally recruited for the study.

Health education was provided before obtaining consent for a newborn to be screened. The duration of the education was approximately 30 min and was based on the mothers' questions. Health education on SCD was provided through a brief interview with a group of mothers. The information included the origin of SCD, the different types of sickle cell status, the importance of clinic visits, and healthy lifestyles. The training was conducted in Swahili and/or French to ensure understanding.

The results of the sickle cell screening had been communicated to all mothers. Newborns who tested positive for SCD were referred to the pediatrician (principal investigator) for further follow-up and advice.

Sample collection and analysis technique

A maximum of 5 ml of blood sample was collected in ethylene diamine tetraacetic acid microtainer tubes from the heel puncture of each newborn in the selected health facilities. The neonatal blood samples were then transported to the laboratory of the Monkole Hospital in Kinshasa (in the DRC) where capillary electrophoresis (using a new generation Capillarys 2 Flex Piercing System [Sebia SA, France]) was performed. The whole blood samples were stored for a maximum of 5 days at 2–8°C, to avoid degradation of the hemoglobins.

The Sebia capillary electrophoresis method involves several steps. First, the primary tubes containing the previously prepared red blood cells are placed on the injection site of the rack. The barcodes are placed facing the reading window. After injection of the sample rack, the barcodes of the primary sample tubes are read by the machine. The samples are then

hemolyzed and diluted with the hemolyzing solution in the reagent cups, with rinsing of the sampling needle between each dilution. The capillaries are washed before injection of the hemolyzed samples into the capillaries, with injection at the anode by aspiration. The different hemoglobin (Hb) fractions then migrate into the capillaries in a basic medium (pH 9.4), allowing their separation and direct detection at the cathode. The migration, which lasts approximately 14 min, is carried out at a high constant voltage (several thousand volts) and at a temperature regulated by the Peltier effect. The reading of the different Hb peaks is performed at 415 nm, corresponding to the wavelength of maximum absorption of Hb. All these steps result in electrophoretic tracings or profiles which are then interpreted by the biologist.

Statistical analysis

Statistical analyses were performed using STATA 16 software (StataCorp, College Station, TX). Proportions were calculated for the different Hb types and the results were presented with a two-sided 95% CI using the Wilson score method with continuity correction.

Ethical considerations

Ethical approval for this study was obtained from the Medical Ethics Committee of the University of Lubumbashi (Approval No. UNILU/CEM/030/2020). Verbal and/or written informed consent was obtained from each respondent with an assurance of confidentiality of the information and the right to withdraw from the study at any time. Participants were advised to understand that participation in the study was voluntary. The researchers ensured the strict confidentiality of all participants' information. Blood samples were collected and sent for genotype confirmation at no cost to the participants and efforts were made to minimize the discomfort of participants during blood sampling.

RESULTS

Neonatal screening for SCD was conducted for 7 months (June–December 2020). As this was a study phase and neonatal screening for SCD is not a health policy in the DRC, the collection of blood samples was carried out according to the availability of resources and for a few hours each day. Six hundred participants were selected and 62 mothers refused to give consent for newborn screening.

Five hundred and eighty-eight blood samples were taken and analyzed from 538 newborns, of which 286 (53.16%) were boys and 271 (46.84%) were girls. All children were black Congolese. The mean chronological age at screening was 0.62 days (0–6 days). None of the newborns were transfused before screening.

The phenotypes were as follows: 369 (68.59%; 95% CI: 64.48%–72.49%) newborns were AA; 141 (26.21%; 95% CI: 22.54%–30.14%) newborns were AS; 27 (5.01%; 95% CI: 3.33%–7.22%) newborns were SS, and 1 (0.19%; 95% CI: 0.00%–1.03%) newborn was AC [Table 1].

DISCUSSION

These results, although limited to the city, have some informational value on the prevalence of genetic hemoglobinopathies in Lubumbashi. We conducted neonatal screening for SCD in five referral maternity units in Lubumbashi city. During the study period, of the 600 mothers who were sensitized in the maternity units selected for sickle cell screening of their newborns, 588 (98%) of them accepted. We believe that this acceptance rate is quite significant and would justify the implementation of systematic neonatal screening for SCD throughout the country.

The present study found that 5.01% of newborns were HbSS (homozygous SCD), 26.21% were HbAS, and 0.19% were HbAC. These results are striking given the high prevalence of SCD (5.01% HbSS) found in the neonatal population in Lubumbashi. This study follows a recent preliminary study by Shongo MY and Mukuku O[8] in which a neonatal screening for SCD in 173 newborns screened in the maternity wards of three health facilities in Lubumbashi reported 12.14% HbAS and 3.47% HbSS. As in the present study, these authors did not find any cases of composite SC heterozygosity in their series, presumably due to the relatively low prevalence of Hb C in the general Congolese population.[6] In the DRC, two other similar studies had already been conducted. The first, carried out on 520 newborns in 5 health facilities in Kisangani city, found that 23.3% of newborns were carriers of the sickle cell trait and 0.96% of homozygous sickle cell.[14] The second carried out in a series of 31,204 newborns recruited throughout the country, reported that 16.9% of newborns were carriers of the sickle cell trait and 1.4% of homozygous sickle cell.[6] The latter noted that there was no statistically significant difference between the different ethno-linguistic groups in the country, but that a high prevalence of the beta S gene was noted in tribes where the prevalence of malaria is high.[6]

A previous study, conducted in the Great Lakes region (Burundi, Rwanda, and Eastern DRC) in four maternity wards

Table 1: Hemoglobin phenotypes of 538 newborns.

Hemoglobin phenotypes	Number (*n*=538)	Percentage (95% confidence interval)
AA	369	68.59 (64.48–72.49)
AS	141	26.21 (22.54–30.14)
SS	27	5.01 (3.33–7.22)
AC	1	0.19 (0.00–1.03)

in a series of 1825 newborns, found 0.11% of HbSS and 3.28% of sickle cell trait. The presence of Hb C was noted in 4 newborns (0.22%).[15] In Gabon, 143 children were heterozygous (15.10%) and 17 HbSS (1.80%) in a series of 947 newborns recruited in two maternity hospitals in Libreville.[16] In Nigeria in Benin City, Odunvbun *et al.*,[17] in a series of 628 recruited neonates, found that 133 (20.6%) were AS, 7 (1.1%) were AC, 18 (2.8%) were SS, and 1 (0.2%) was SC. In view of these results, it is preferable to introduce a systematic screening of all newborns instead of targeted screening (limited to screening newborns of mothers who know their Hb phenotypes). Odunvbun *et al.*[17] pointed out that mothers' lack of knowledge of their phenotype may have led to the high level of marriage among sickle cell trait carriers, resulting in the high prevalence of SCD in their community. The impact of information and awareness on SCD, in the general population and particularly among young adolescents and adults, is very significant. This is illustrated by the example of a long-running information and education campaign in Bahrain in the Middle East, which reduced the rate of carriers of SCD by 60% in 18 years.[18]

SCD remains unknown and ignored by the Congolese population in general and is most often equated with witchcraft; this turns patients away from the hospital, often sending them to charlatans. The disease is ignored by many, leading to stigmatization of the patients, rejection, and mockery by their peers, and by their entourage in general. Patients and their families are left to their own devices, living in unbearable and unacceptable conditions of physical and psychological suffering. The financial burden of SCD puts a strain on families who are often broken. The various methods of screening for SCD are almost non-existent in the hospitals in Lubumbashi; only a few health centers or private laboratories offer it.

CONCLUSION

SCD is very common among newborns in Lubumbashi. The present study determined the prevalence of SCD during newborn screening in Lubumbashi. The conduct of premarital counseling is essential to reduce the prevalence of this hemoglobinopathy which is very high (5.01% Hb SS). Systematic newborn screening in all maternity wards in the country would help to assess the prevalence at the national level and improve the quality of life of SCD children.

Data availability

The dataset used to support the findings of this study is available from the corresponding author on request.

Disclosure

The abstract was presented at the "61st Annual Scientific Meeting of the British Society for Hematology" (virtual in April 2021).

Ethical approval

Ethical approval for this study was obtained from the Medical Ethics Committee of the University of Lubumbashi (Approval No. UNILU/CEM/030/2020).

Declaration of patient consent

Patient's consent not required as patient's identity is not disclosed or compromised.

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Nil.

Conflicts of interest

There are no conflicts of interest.

Use of artificial intelligence (AI)-assisted technology for manuscript preparation

The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript and no images were manipulated using AI.

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