Hospital Prevalence of Sickle Cell Disease in Children Under 5 Years of Age in a Region of the Democratic Republic of Congo

Abdala Kingwengwe Aimé
Department of Pediatrics, Faculty of Medicine, University of Kindu, Democratic Republic of Congo; Disease Prevention and Control Unit, Faculty of Medicine, University of Kindu, Democratic Republic of Congo; Department of Pediatrics, Faculty of Medicine, University of Lubumbashi, Democratic Republic of Congo

Shongo Ya Pongombo Mick
Department of Pediatrics, Faculty of Medicine, University of Lubumbashi, Democratic Republic of Congo

Mudekereza Musimwa Aimée
Department of Pediatrics, Faculty of Medicine, University of Lubumbashi, Democratic Republic of Congo

Tshilolo Muepu Léon
CEFA/Mother-child Hospital Center of Monkole, Kinshasa, Democratic Republic of Congo

Shindano Mwamba Etienne
Department of Pediatrics, Faculty of Medicine, University of Kindu, Democratic Republic of Congo; Disease Prevention and Control Unit, Faculty of Medicine, University of Kindu, Democratic Republic of Congo

Wembonyama Okitotsho Stanis
Department of Pediatrics, Faculty of Medicine, University of Lubumbashi, Democratic Republic of Congo

Abstract

Background: The burden of sickle cell disease in hospitals is less described in both children and adults where there is a lack of universal screening programs. This is more observed in low-income countries and compromises the life expectancy of people with unrecognized major sickle cell disease. The objective of this study was to estimate the more or less concrete burden of sickle cell disease in pediatric hospitals, mainly in children under 5 years of age.

Materials & methods: To do this, a cross-sectional and descriptive survey was carried out at the level of the pediatric services of 5 health facilities of the City of Kindu, capital of the province of Maniema in the Democratic Republic of the Congo from December 2, 2019 to October 15, 2020, that to say 10 months. It consisted mainly in the systematic screening of the electrophoretic profile of children under 5 admitted to the said health facilities using a rapid test.

Results: The analyzes showed that the hospital prevalence of major sickle cell disease was 12.7%. The mean age of children with major sickle cell anemia was 41 ± 18 months. The median age was 48 months with the extreme ages 2 and 59 months. The 48 to 59 months age group was represented with 56.1% of children with SS sickle cell disease. The prevalence of sickle cell status was significantly associated with age group (p <0.0001). The sex ratio M/F was 1.1. The sickle cell status was independent of the sex of the child.

Conclusion: The findings of this study show that the burden of sickle cell disease in pediatric hospitals and mainly in children under 5 years of age is underestimated in the absence of systematic screening. Faced with the delay in the implementation of universal screening...
in Africa, systematic hospital screening of all children and mainly those under 5 years of age using rapid tests will improve diagnosis and life expectancy of patients with major sickle cell anaemia.

Introduction

Sickle cell disease is now considered the first and most common genetic hemoglobin disorder in the world [1,2]. Most statistical data on sickle cell disease is estimates. Access to information on the disease is difficult in several countries. Existing information most often comes from hospital data and not from the general population [1,2]. Sickle cell disease is one of the main causes of morbidity and mortality in children under 5 years of age. Its weight remains underestimated due to lack of universal screening in many low-income countries [3,4].

The prevalence of sickle cell disease depends on that of sickle cell trait. For a prevalence of sickle cell trait greater than 20%, the prevalence of homozygous sickle cell disease is estimated to be at least 2% [1]. Worldwide, the prevalence of sickle cell trait reaches, with regional differences, up to 45% [5]. The regions with a high prevalence of sickle cell disease are successively intertropical Africa, the Arab-Indian zone and the Mediterranean basin [6]. Recent statistics estimate that each year, approximately 300,000 children are born with the major form of the disease [1,7]. This figure could increase by 2050 and reach 500,000 annual cases due to global population growth [3].

Europe has two regional facets of sickle cell disease. In some regions, the disease is autochthonous (Mediterranean basin) and in other regions, it is mainly linked to the immigration of people from the original centers. In regions of the Mediterranean basin, the prevalence of sickle cell trait varies between 1 and 5% [8].

In America, sickle cell disease is linked to the slave trade and migratory flows of recent decades. This vision means that the extent of the disease is assessed more in African-American populations than in the general population. Overall, the prevalence of sickle cell trait is less than 1% in the general population of the American continent [9].

In Europe as in America, the hospital prevalence of the major form of the disease is less than 1% [10,11]. The data reported in these regions are reliable because these regions have effective control programs and screening for the disease is systematic among populations at risk and even among all newborns [12,13,14].

In Asia, mainly in the Arab-Indian Peninsula, the prevalence of sickle cell disease in the general population of the most affected regions varies up to 22% for sickle cell trait and 1.2% for the major form [15,16,17]. In a hospital setting, a study conducted in India reported between 10 and 15% of subjects with major sickle cell syndrome among children under 5 years of age [18].

In Africa, sickle cell disease spreads across the entire continent with a decrease in prevalence as one moves away from the center of the continent. This gives rise to an area called the “sicklemic belt” which extends between the 15th parallel north latitude south of the Sahara and the 20th parallel south latitude north of the Zambezi River [19]. The continental distribution of sickle cell disease in Africa displays variations across continent regions, countries and ethnicities. Depending on the region, the frequency of sickle cell trait is estimated as follows [5,19]:

- In North Africa: 1 to 2%;
- In West Africa: 6 to 30%);
- In East Africa: up to 45% in parts of Uganda;
- In southern Africa: less than 1%;
- In Central Africa: 20 to 40%.

The hospital prevalence of sickle cell disease in Africa is less described and varies depending on two major elements; the prevalence of the disease in the general population and the level of implementation of case detection. African studies which have determined the hospital prevalence of subjects with major sickle cell syndrome in pediatric settings report a prevalence of between 1.3% and 3.5% [20,21,22,23].

The gene carriers is estimated at 17.9% in the neonatal population with variations according to the provinces. The prevalence of major sickle cell syndrome is estimated at 1.9% of newborns and can reach up to 2.5% in certain provinces [24]. In a hospital setting, the WHO estimates that 12% of children admitted to pediatric departments in the DRC have major sickle cell syndrome [1].

In Maniema, estimated data report that the prevalence of sickle cell disease in the neonatal population would be 15 to 28.7% of β genes carriers including 1.3 to 1.9% of newborns with major sickle cell syndrome [24,25]. In terms of the management of sickle cell disease, this province does not yet have any structure specialized in the treatment and monitoring of patients [26]. To date, there are no studies that have determined the hospital prevalence of this pathology in the province of Maniema in general and the town of Kindu in particular. This lack of epidemiological information does not allow for improvement in the management of the disease in this environment. The objective of the present study was to estimate the hospital prevalence of sickle cell disease in pediatric hospitals, mainly among hospitalized children under 5 years of age.
Methodology
This was a cross-sectional and descriptive study, the collection of which was carried out at the level of the pediatric services of 5 health facilities in the City of Kindu, namely the Kindu Provincial Reference Hospital, the General Hospital reference center of Alunguli, the Kitulizo Hospital Center, the Lumbulumbu Hospital Center and the CEPAC-Brazza Reference Health Center. The reception capacity of these health facilities is:
- Kindu provincial referral hospital: 250 beds including 100 for the pediatric department;
- Alunguli General Reference Hospital: 180 beds including 50 for the pediatric department;
- Kitulizo hospital center: 140 beds including 55 for the pediatric department;
- Lumbulumbu hospital center: 120 beds including 25 for the pediatric department;
- CEPAC-Brazza reference health center: 70 beds including 20 for the pediatric department.

The City of Kindu is the capital of the Maniema province in the Democratic Republic of Congo. It has approximately 391,143 inhabitants. The child population is generally estimated at around 187,749 children, or 48% of the total population. Among these children, 73,926 are under 5 years old and they represent 19% of the total population [27].

The study took place from December 2, 2019 to October 15, 2020, over a period of 10 months. We selected as the study population all children under 5 years old admitted to the 5 health facilities selected. Sampling was done in proportion to pediatric admissions that met the selection criteria set for this study.

The inclusion criteria for the study were admission to the pediatric department of one of the FOSAs selected for the study, age less than 5 years, absence of a history of transfusion within 4 months preceding recruitment, the concordance of the biological results of the confirmatory examinations and the informed consent of the guardian.

The sample was constituted according to the following procedure:
- Carrying out the HemoTypeSC rapid test on all children under 5 years old admitted to our study sites;
- Collection of blood smears from all participants on blotting papers for confirmatory analysis of their electrophoretic hemoglobin profile at the laboratory of the Health Training and Support Center (CEFA)/Mother-Child Hospital Center of Monkole in Kinshasa. In this laboratory, the samples successively underwent two diagnostic tests, namely isoelectrofocusing then capillary electrophoresis of hemoglobin.

HemoTypeSC is a rapid diagnostic test incorporating monoclonal antibodies for the detection of hemoglobin A, hemoglobin S, and hemoglobin C [28]. The primary study variable was the participants’ hemoglobin electrophoretic profile. In this study, this profile is represented by the following expressions:
- Normal subject: any subject whose hemoglobin electrophoretic phenotype is AA. It is also called homozygous AA;
- Subject with sickle cell disease: any subject carrying the βs gene. This status includes SS homozygotes, AS or AC heterozygotes and compound heterozygotes;
- Carrier of the sickle cell trait: any AS or AC heterozygous subject;
- Subject with major sickle cell syndrome: any homozygous SS or composite heterozygous subject;
- SS sickle cell or SS homozygous sickle cell: any SS homozygous subject.

The processing and analysis of the collected data were carried out with the XLSTAT 2016 software. The univariate analyzes made it possible to determine the prevalence, the distribution of children with major sickle cell syndrome according to age and sex and finally the calculation measures of central tendency (mean, mode, median). Bivariate analyzes were used to investigate the dependence between study variables (age and sex) and major sickle cell status. The AA subjects served as a comparison group for the calculation of the dependence test at the 5% significance level.

This study was conducted in compliance with both national and international ethical rules. She received a favorable opinion from the Medical Ethics Committee of the University of Lubumbashi through her letter No UNILU/CEM/023/2019.

Results
A total of 448 children under 5 years old, including 192 girls and 256 boys, participated in the study after informed consent from their guardians. It appears in Table 1 that the overall hospital prevalence of sickle cell disease in children under 5 years old is 31.9%, including 12.7% in its homozygous
SS form and 19.2% in the heterozygous AS and AC form. (Table 1).

Table 1: Distribution of Respondents According to Their Hemoglobin Electrophoretic Profile

<table>
<thead>
<tr>
<th>Electrophoretic profile of Hb</th>
<th>Effective</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>AA</td>
<td>305</td>
<td>68.1</td>
</tr>
<tr>
<td>A.S.</td>
<td>85</td>
<td>19.0</td>
</tr>
<tr>
<td>SS</td>
<td>57</td>
<td>12.7</td>
</tr>
<tr>
<td>AC</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>Total</td>
<td>448</td>
<td>100.0</td>
</tr>
</tbody>
</table>

Table 2 shows that the age group of 48 to 59 months is the most represented among SS sickle cell children screened in hospitals. The mean age was 41 ± 18 months. The median age encountered was 48 months with extreme ages of 2 and 59 months. A statistical dependence was observed between major sickle cell status and age. Major sickle cell status is more prevalent in the age group 48 to 59 months (Table 2).

Table 2: Distribution of Respondents According to Age and Sickle Cell Status

<table>
<thead>
<tr>
<th>Age (months)</th>
<th>SS homozygotes</th>
<th>AA Topics</th>
<th>Total</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>[0 - 11]</td>
<td>6 (10.5)</td>
<td>140 (45.9)</td>
<td>146 (40.3)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>[12 - 23]</td>
<td>8 (14.0)</td>
<td>65 (21.3)</td>
<td>73 (20.2)</td>
<td></td>
</tr>
<tr>
<td>[24 - 35]</td>
<td>6 (10.5)</td>
<td>30 (9.8)</td>
<td>36 (9.9)</td>
<td></td>
</tr>
<tr>
<td>[36 - 47]</td>
<td>5 (8.8)</td>
<td>25 (8.2)</td>
<td>30 (8.3)</td>
<td></td>
</tr>
<tr>
<td>[48 - 59]</td>
<td>32 (56.1)</td>
<td>45 (14.8)</td>
<td>77 (21.3)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>57</td>
<td>305</td>
<td>362</td>
<td></td>
</tr>
</tbody>
</table>

Table 3: Distribution of Respondents According to Sex and Sickle Cell Status

<table>
<thead>
<tr>
<th>Sex</th>
<th>SS homozygotes</th>
<th>AA Topics</th>
<th>Total</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Feminine</td>
<td>27 (47.0)</td>
<td>132 (43.3)</td>
<td>159 (43.9)</td>
<td>0.568</td>
</tr>
<tr>
<td>Male</td>
<td>30 (53.0)</td>
<td>173 (56.7)</td>
<td>203 (56.1)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>57</td>
<td>305</td>
<td>362</td>
<td></td>
</tr>
</tbody>
</table>

Discussion

This study aimed to estimate the prevalence of sickle cell disease in pediatric hospitals, mainly in children under 5 years old. Knowledge of this prevalence in hospitals, based on systematic screening, could contribute to the improvement of intra- and extrahospital care in the city of Kindu in particular and the province of Maniema in general. In this study, the hospital prevalence of children under 5 years of age carrying the $\beta$ s gene was 31.9%, including 12.7% SS homozygotes and 19.2% heterozygotes carrying the trait. In Europe and America, regions with low sickle cell prevalence, the prevalence of the major form of the disease in hospitals is less than 1% [10,11].

In the Arab-Indian Peninsula, one of the regions with a high prevalence of sickle cell disease, Dipty reports a hospital prevalence of major sickle cell disease of 10 to 15% [18]. Camara, in Guinea, found a hospital frequency of 7.8% of children with major sickle cell syndrome of all ages [29]. This result is observed in a context of children followed after screening for their status and is similar to our observations. Its low prevalence could be explained by the low distribution of sickle cell disease in Guinea compared to the DRC [6].

Other African studies, carried out outside of systematic screening, have also determined the hospital prevalence of major sickle cell disease in pediatric settings. They report a prevalence of between 1.3% and 3.5% [20,21,22,23]. Their observations are lower than those of our series. The prevalence of homozygous SS children found in our series corroborates WHO estimates of the hospital prevalence of major sickle cell disease in pediatric settings in the DR Congo, which is 12% [1]. Still in the DRC, 3 studies were carried out on the prevalence of sickle cell disease in hospitals: Katamea in Lubumbashi in particular observed a prevalence of 21.2% of $\beta$ s gene carriers among children aged 0 to 6 months, including 10.9% SS homozygotes [30]; two studies carried out in hospitals in Bukavu and Goma reported a respective frequency of 2.8% and 3.4% of children with sickle cell SS among admissions to pediatric departments [31,32]. In these last two studies, carried out outside a systematic screening context, the prevalence of sickle cell disease in pediatric hospitals is low compared to our series. This is the tip of the iceberg as it is observed only from children with...
known major sickle cell disease before admission. The systematic screening carried out in our series revealed the cliché.

In our series, the age group of 48 to 59 months was the most represented (56.1%) among children with SS sickle cell disease screened in hospital. The mean age was 41 ± 18 months. The youngest subject with major sickle cell disease in our series was 2 months old. The prevalence of sickle cell syndrome in the age group 48 to 59 months is statistically significant (p < 0.0001). This observation can be explained by the drop in fetal hemoglobin level which inversely decreases with age. This drop in fetal hemoglobin levels increases the morbidity of subjects with major sickle cell disease [33,34]. On the other hand, other authors believe that several subjects with major sickle cell disease die before the age of two years following severe infectious complications without their status being known due to lack of early detection [35,36]. Shongo, in his study carried out among SS sickle cell patients under 5 years old followed on an outpatient basis in a specific care center, found that the age group 36 to 59 months was the most represented with 48.8% [37]. The mean age in his series was 39.12 months ± 16.30 [37]. The youngest of his patients was 6 months old [37]. Our observations are similar to those made by Shongo’s study. Referring to the hypothesis of Douamba and Tshilolo who think that several children with major sickle cell disease would die before the age of two without their status being known [35,36], it is obvious that when neonatal screening and patient monitoring are well organized in settings with limited resources, the morbidity of sickle cell patients depending on age groups may change. For illustration, Dipty reports in its series that 56% of subjects were less than 36 months old [18]. The systematic screening carried out during our study, although only concerned children who met the inclusion criteria, made it possible to detect cases of sickle cell disease early before the age of 2 years, contrary to our previous observations [38]. There is therefore an interest in strengthening early detection of the disease to improve the life expectancy of patients with major sickle cell disease.

**Conclusion**

The hospital prevalence of major sickle cell disease in our study is high and supports WHO estimates. Thanks to systematic screening, it appears that the burden of disease in pediatric hospitals and mainly in children under 5 years old is underestimated. The age group of 48 to 59 months is statistically the most represented among children under 5 years old with major sickle cell syndrome. Faced with the delay in the implementation of universal screening in the African environment, systematic hospital screening of all children and mainly those under 5 years old using rapid tests will allow an improvement in the life expectancy of patients with major sickle cell disease. These tests should be less expensive and available everywhere to meet the requirements of standard diagnostic means.

**Conflict of Interest**

The authors declare no conflict of interest.

**Contribution of the Authors**

Abdala KA designed, conducted the study and wrote the article. SYPM guided the writing and editing of the article. MMA has made substantial corrections to the article. TML, SME and WOS supervised all stages of the study and then corrected the final version of the article.

**Existing Knowledge**

Patchy prevalence of sickle cell disease in Central Africa.

**Contribution of the Study**

The study has just estimated, for the first time, the concrete hospital prevalence of sickle cell disease in children under 5 years old in a region of the DRC.

**Acknowledgement**

Team that helped recruit respondents. Guardians who consented to the children's participation in the survey. The Monkole Mother-Child Hospital Center for the analysis of electrophoresis samples.

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