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BRIEF COMMUNICATION

Importance of early detection of hemoglobinopathies in the pediatric population in developing countries

Importancia de la detección temprana de hemoglobinopatias en la población pediátrica en países en desarrollo

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What do we know about the subject matter of this study?

Hemoglobinopathies are common monogenic recessive diseases. Identifying patients' characteristics supports the recommendation for implementing a screening program in developing countries with a high prevalence.

What does this study contribute to what is already known?

In this retrospective cohort of 152 patients who underwent capillary electrophoresis, 42.7% presented some type of hemoglobinopathy, where HbS was the most frequent. The age of diagnosis was over 7 years and the test was usually requested by a hematology specialist.

Abstract

Objective: The objective of this study is to spread awareness among health personnel about the importance of early detection of hemoglobinopathies since it is the most frequent monogenic recessive disorder worldwide. **Patients and Method:** Retrospective study of the results of capillary electrophoresis (CE) of 152 patients aged between 0 and 18 years who were evaluated in 2017 due to suspected hemoglobinopathies in a University Hospital in Colombia. The information was collected from medical records and the Hematology and Hemostasis Laboratory, ensuring data privacy and approved by the local Ethics Committee. **Results:** Of 152 patients, 48.6% were aged between 7 and 18. The frequency of hemoglobinopathies was 42.7%. The most frequent hemoglobin variant was the sickle cell trait (Hb S) with 14.5%. The hematologist was the professional who most frequently requested CE. **Discussion:** We found that hemoglobinopathies are usually diagnosed late in pediatric patients. This may favor complications and progression of the disease and increase healthcare costs. More information and education are required for general physicians and pediatricians in order to achieve early diagnosis.

Keywords:
Neonatal Screening; Hemoglobinopathies; Sickle Cell Anemia; Primary Prevention; sickle cell trait

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Abbreviations

CE: capillary electrophoresis
Hb: hemoglobin
HPLC: High-Performance Liquid Chromatography
WHO: World Health Organization

Introduction

Hemoglobinopathies include all genetic disorders of hemoglobin protein (Hb), in which genetic variations cause an abnormal structure of globin chains and persistence of fetal Hb. These disorders account for most of the recessive monogenic diseases in the world[2] since more than 300,000 children are born each year with some hemoglobinopathy, 83% with sickle cell disease, and 17% with thalassemia[3]. Hemoglobinopathies cause 3.4% of deaths in children under 5 years of age[2].

The Latin American population is not often screened for Hb disorders. Venezuela presented a prevalence of hemoglobinopathies around 1.97%, 1.6% in Brazil, and 1.26% in Costa Rica[4]. In Colombia, these disorders are considered endemic diseases[5]. In 2016, a descriptive study in eight capital cities in Colombia showed 1.3% prevalence of Hb variants, where hemoglobin S (Hb) was the most common, followed by Hb C. Barranquilla, Cartagena, and Cali were the cities with the highest prevalence[6].

In 2017, Colombia's Biweekly National Epidemiological Report showed that Hb disorders in childhood are diagnosed around the age of 9 years[7]. This leads to increased health costs, deteriorating quality of life, higher mortality due to infections, cardiopulmonary and musculoskeletal conditions, increased pain and aplastic crises, and slow growth, among others[5]. For this reason, the World Health Organization (WHO) recommends neonatal screening for hemoglobinopathies in populations at risk which reduces morbidity and mortality in early childhood[8].

The objective of this study is to raise awareness among health professionals about the importance of early detection of hemoglobinopathies in the pediatric population in a developing country like Colombia. The diagnostic technique used is capillary electrophoresis (CE), since high-performance liquid chromatography (HPLC) is not yet available. We reported the prevalence of different types of hemoglobinopathies in a sample of at-risk pediatric patients who underwent capillary electrophoresis (CE) at a university hospital.

Patients and Method

Retrospective study of 152 patients aged between 0 and 18 years who underwent CE (CAPILLARYS 2 FLEX PIERCING, Sebia, France) for the diagnosis of Hb disorders in a University Hospital in Colombia.

The Hb analysis through CE was based on the separation of different Hb fractions according to their difference in electrical charges. The Hb chains were separated in a negatively charged silica tube, which offers significant advantages such as greater differentiation of hemoglobin variants, low volume of samples required, and automation of test performance with a higher number of samples processed in a shorter time[9]. We gathered information from the medical records and the record of the Special Hematology and Hemostasis Laboratory of our University Hospital throughout the study.

All information was collected ensuring data privacy and following standards of good practice in clinical research and approved by the Ethics Committee. Statistical analyses were performed using Stata v. 14® software.

Results

152 patients were included in this study, 57% of them were female. The frequency according to age distribution was ≤ 28 days in 4 children; 28 days to 3 months in 7 children; 4 to 12 months in 19 children; 13 to 24 months in 14 children; 3 to 6 years in 34 children; and 7 to 18 years in 74 children. 98.1% had health insurance. The physicians who requested CE were a hematologist (107 tests; age 7.3 ± 5.07 years), a pediatrician (40 tests; age 5.9 ± 5.4 years), and a neonatologist (5 tests; age 2.6 ± 4.7 years). The reasons for CE were anemia study (102 children), hemoglobinopathy monitoring (32 children), screening (10 children), and as a family history study (8 children). In 42.7% of the cases, there was some type of hemoglobinopathy, where the sickle cell trait (Hb S) was the most frequent, followed by sickle cell disease (Hb SS) and Hb C (see Figure 1).

Discussion

In this study, most CE tests were performed on children aged between 7 and 18, who were screened for anemia. These patients were not pre-screened despite having access to the test due to health insurance coverage. There was a similar pattern of sickle cell disease in the epidemiological bulletin of the same year, where the mean age of diagnosis was 9 years[7]. The most common hemoglobinopathy was sickle cell trait (Hb S) accounting for 14.5%, followed by sickle cell disease (Hb SS) with 11.8%, which was similar to previous national and international studies[1,2,6,10,11]. It is worth mentioning that the EC results reported in this study

were calculated for children at risk who are being studied for anemia and not for screening purposes, therefore, the prevalence may be higher compared with other hospitals in Colombia. In addition, since this is a University Hospital where many complex cases are referred for specialized studies that are not available in other laboratories, the prevalence may be higher. Qualitative hemoglobinopathies were not evaluated in this study, however, since they were of lower prevalence, they did not significantly affect the research.

Global migration trends have changed the epidemiology of hemoglobinopathies. Hb disorders first appeared in Africa, Asia, and the Mediterranean Basin and have spread worldwide due to the migration of these groups[12]. This has led to a change in the demographic scene and has increased the occurrence of this condition in areas where prevalence is low such as North America and Europe[13]. According to the WHO's epidemiological registry, 71% of the world's countries present hemoglobinopathies, which represents a major health problem[3]. These migratory trends have been especially marked in Latin America and the Caribbean[12], which may explain the high prevalence in countries such as Venezuela, Brazil, Colombia, and Costa Rica. The current migration of Venezuelans to neighboring countries may generate a significant increase in hemoglobinopathies in other populations with lower or no previous prevalence[4].

Sickle cell anemia is the leading structural hemoglobinopathy. The best-known causes of morbidity and mortality due to these disorders are infection (33%-38%), followed by stroke (9.8%) and splenic sequestration (6.6%)[14-16]. It has been reported that in patients aged between 1 and 3 years, infections present the highest increase, with 35 to 50% mortality rate due to sepsis, mainly in children under 3 years old[17]. In developed countries, survival has improved due to timely diagnosis through neonatal screening, since it allows the early implementation of prophylaxis, vaccination, and penicillin treatment[18,19].

Despite the above, we found in this study that the CE used for both screening and diagnosis of hemoglobinopathies was mainly prescribed by the hematologist (70.4%), who was the third physician that evaluated the patient, after the neonatologist and pediatrician. This represents the loss of opportunity for early diagnosis. In contrast, newborn screening favors survival and improved the quality of life for pediatric patients[5]. Therefore, we hope that this study will raise awareness among health professionals to suspect these disorders in pediatric patients with anemia and promote early diagnosis in the primary care setting, or better still as screening, avoiding future complications as mentioned before[7,11,20].

In conclusion, hemoglobinopathies are diagnosed long after the age of 7. The sickle cell trait was the most frequent followed by sickle cell disease, which puts at risk of morbidity the vulnerable population with unfavorable outcomes. Despite knowing the importance of early detection of these disorders, most health professionals who first evaluate the patient did not indicate CE for screening and diagnosis of hemoglobinopathies. Therefore, we recommend the implementation of protocols that include mandatory screening in children under three months, to reduce the complications associated with these Hb disorders and improve the quality of life of these patients. In Colombia, the only mandatory screening that has been adequately implemented and regulated in newborns is the thyroid-stimulating hormone for the diagnosis of congenital hypothyroi-

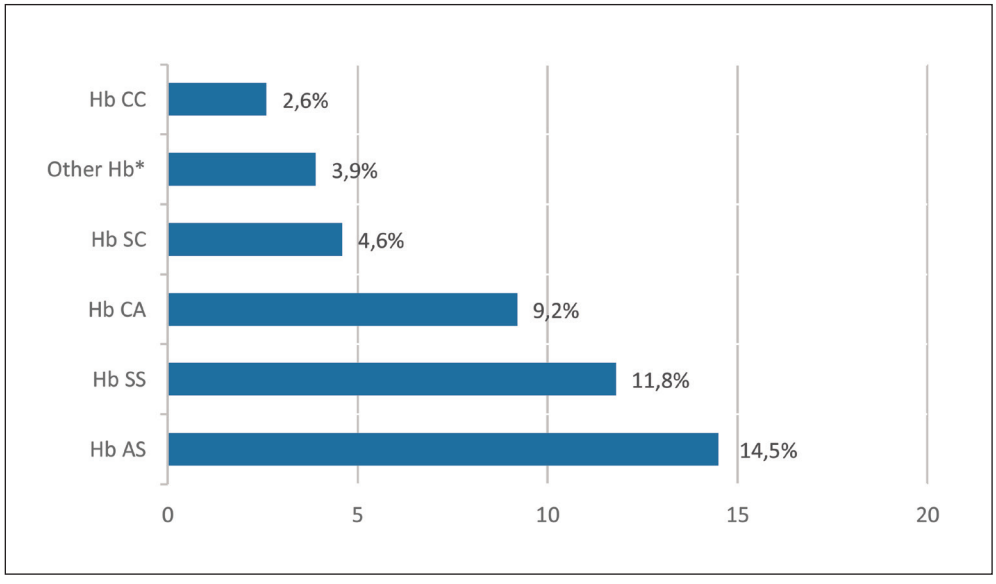

Figure 1. Distribution of hemoglobinopathies diagnosed by capillary electrophoresis in a hospital of Cali, Colombia.

dism. More advanced techniques such as HPLC have not yet been implemented for the diagnosis of Hb disorders.

Ethical Responsibilities

Human Beings and animals protection: Disclosure the authors state that the procedures were followed according to the Declaration of Helsinki and the World Medical Association regarding human experimentation developed for the medical community.

Data confidentiality: The authors state that they have followed the protocols of their Center and Local regulations on the publication of patient data.

Rights to privacy and informed consent: The authors state that the information has been obtained anonymously from previous data, therefore, Research Ethics Committee, in its discretion, has exempted from obtaining an informed consent, which is recorded in the respective form.

Conflicts of Interest

Authors declare no conflict of interest regarding the present study.

Financial Disclosure

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