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Original article

Follow-up of children with hemoglobinopathies diagnosed by the Brazilian Neonatal Screening Program in the State of Pernambuco

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ABSTRACT

Objective: To determine the geographical distribution of hemoglobinopathies in the State of Pernambuco, to characterize the children with these diseases and to describe factors associated with their follow-up at the referral center during the period from 2003 to 2010.
Methods: A retrospective, cross-sectional, descriptive study was carried out of 275 medical records from a total of 302 children with hemoglobinopathies diagnosed by the National Neonatal Screening Program in the State of Pernambuco in the study period. Microsoft Excel was used for data processing and analysis. The chi-square and the Fisher test were used for statistical analysis. The level of significance was set at 5%. Terra View software was used to analyze the geographical distribution of hemoglobinopathies in the State.
Results: A total of 8.9% of the cases of hemoglobinopathies detected in the period were not followed up at the referral center. For the mothers of children with diseases, this was their second or third or more pregnancy in 64.2% and 30.2%, respectively. Regarding the influence of region of residence and regular medical appointments, the study demonstrated that children from the Zona da Mata, Sertão and Vale do São Francisco regions did not attend 45.2%, 50% and 55.6% of their appointments in the outpatient department, respectively.
Conclusions: This study shows that a significant number of children do not begin consultations in the outpatient clinic and even those who started treatment early and who have the most severe form of the disease, usually miss medical appointments.

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Introduction

Hemoglobinopathies result from mutations in the genes that encode the alpha (α) and beta (β) globin chains of the hemoglobin molecule (Hb). The abnormal Hb S is the result of a mutation that leads to the replacement of a glutamic acid with a valine at position 6 of the β chain, with consequent changes in the Hb molecule.[1]

In general, all symptomatic clinical forms of the presence of the Hb S gene, either homozygosis or in combination with another variant hemoglobin such as Hb C, or Hb D or in association with the β thalassemia gene are known as sickle cell disease (SCD). These are the most prevalent forms of all hemoglobinopathies and have the greatest impact owing to the seriousness of clinical manifestations.[2–4] Sickle cell anemia is the form of the disease characterized by Hb S homozygosis inherited from both parents (Hb SS).[5]

The World Health Organization (WHO) estimates that 270 million people carry genes determining variant hemoglobins and that every year 300,000 children are born with SCD.[6] It is the most prevalent hereditary disease in Brazil, affecting 25,000–30,000 people, with approximately 3500 children born with SCD annually. In the State of Pernambuco, the incidence is 1:1400.[7] The disease is thus a public health issue, associated with high infant morbidity and demands regular medical care, adequate housing and nutrition, and general health care.[8]

The disease's clinical variability results from a combination of hereditary and environmental factors. A newborn with SCD is generally asymptomatic due to the protective effect of fetal hemoglobin (Hb F) which, during this period of life, represents around 80% of the total hemoglobin. With the replacement of Hb F by an increase in Hb S, clinical manifestations begin to appear,[9] usually starting at the age of six months and lasting throughout the patient's life.[5,10]

The first years are marked by hemolytic anemia and by vaso-occlusive episodes, dactylitis (inflammation of fingers or toes) or hand-foot syndrome, splenic hypofunction or sequestration, and a higher susceptibility to infections.[9]

Other clinical manifestations may affect SCD children, such as thoracic syndrome, cognitive problems, priapism (which may lead to sexual impotence) and damage to organs such as the kidneys, the lungs and the eyes, diminishing quality of life, generating incapacitation, and frequent stays in hospital for treatment or surgical procedures.[11]

Neonatal diagnosis, early prophylactic treatment with penicillin, prophylactic vaccination, follow-up by specialized services with periodic clinical evaluations, hospitalization in situations of risk, and early identification of splenic sequestration by mothers and caregivers have contributed to a reduction in mortality from 25% to approximately 3% in the first five years of life.[8,12]

The National Neonatal Screening Program (NNSP), created by Resolution GM/MS no. 822/01,[13] enabled early diagnosis, treatment and follow-up of hemoglobinopathies. In the State of Pernambuco, according to Resolution GM nº. 452, of October 18, 2001[14] children with the diagnosis of SCD have been sent to a referral center since 2002 to immediately start treatment in a specialized multidisciplinary outpatient department and a specialized clinic.[15]

The NNSP includes early treatment and regular outpatient appointments of children after neonatal diagnosis.[13,16] It is, however, difficult to achieve this, as several factors lead patients to miss medical consultations. An understanding of what hinders treatment has proved a challenge, as there has been little research on children's follow-up at the referral center after diagnosis at neonatal screening.

The aims of this study were to determine the geographic distribution of hemoglobinopathies in the State of Pernambuco, to characterize the children affected and to describe factors associated to the follow-up at the referral center in the period from 2003 to 2010.

Methods

A retrospective, cross-sectional, descriptive study was carried out of 275 (91.5%) medical records of a total of 302 children with hemoglobinopathies as diagnosed by the NNSP in the State of Pernambuco in the period from 2003 to 2010, who started treatment in the referral center, located at the Pernambuco Hematology and Hemotherapy Foundation (HEMOPE).

According to Datasus,[17] Pernambuco has an area of 98,311 km^2 and a population of 8,810,318. Between 2003 and 2010, a total of 1,166,189 live births occurred in Pernambuco and 605,632 newborns were screened at public health care clinics.

The drawing of blood samples for neonatal screening is carried out at health care units located around the State. Blood samples are then taken to the Pernambuco Central Laboratory (LACEN), where they are processed and analyzed. Positive results for hemoglobinopathies are sent to the Neonatal Screening Referral Service, which refers the cases to HEMOPE, the only referral center in the state that performs treatment and regular outpatient follow-ups in a specialized multidisciplinary outpatient department.

For this study, data collection initially used the LACEN database; the NNSP identified 302 children with hemoglobinopathies. The records of 275 were found at the referral center and several factors were analyzed: diagnosis, region of residence, socioeconomic status of the family, age at first medical appointment, regularity of medical appointments, number of births to the child's mother, and the existence of siblings with hemoglobinopathies. Subsequently, the geographic distribution of the disease in the State was analyzed.

Microsoft Excel was used for data processing and analysis. The chi-square and the Fisher tests were used for statistical analysis. The level of significance was set at 5% (p-value < 0.05). Terra View software[18] was used to analyze the geographical distribution of hemoglobinopathies in the State.

This study was approved by the Human Research Ethics Committee of the Prof. Fernando Figueira Institute for Integral Medicine (IMIP) and by the Pernambuco Hematology and Hemotherapy Foundation (HEMOPE) (protocols nº. 2084-11 and 043/2011).