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Original article

Trends in mortality and hospital admissions of sickle cell disease patients before and after the newborn screening program in Maranhão, Brazil

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ABSTRACT

Objective: To assess the impact of the implementation of neonatal screening on hospitalization and death rates due to sickle cell disease in patients from the state of Maranhão, Brazil.

Methods: A descriptive study was performed of all inpatients and deaths of patients with a diagnosis of sickle cell disease in Maranhão between 1999 and 2012. Data were collected from the Hospital Information System of the Brazilian National Health Service (SUS) and the Death Information System of the Ministry of Health. The implementation of newborn screening tests in Maranhão took place in 2005, and so the periods 1999–2005 (pre) and 2006–2012 (post) were analyzed for trend analysis using a multiple linear regression model. Fisher's exact test was used for the analysis of categorical variables and the Kruskal–Wallis test for continuous variables.

Results: The rate of hospitalization increased from 0.315 (pre) to 1.832 (post), indicating 5.82 times more admissions (p-value = 0.04). The mortality rate increased from 0.115 to 0.216, that is 1.88 times higher, but this was not statistically significant (p-value = 0.586). The median age at admission dropped from 11.4 years to 8.7 years (p-value = 0.0002), whereas the median age at death increased from 10 years to 14 years (p-value = 0.665).

Conclusion: The increases in the rates of hospitalization and death after the implementation of neonatal screening suggests that previously there was an underdiagnosis of sickle cell disease and that screening, along with other factors, increased "visibility" in the state of Maranhão.

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Introduction

Hemoglobin (Hb) S originated in Africa where the mutation in the beta-globin gene was advantageous insomuch as heterozygotes have more resistance against malaria.[1] In Brazil, sickle cell disease (SCD), the most prevalent hereditary disease, affects the black population most. It is estimated that about 45% of the Brazilian population and 72% of the population of the state of Maranhão is of African descendancy. Moreover, in Brazil there are 25–30,000 SCD patients with 3500 new cases diagnosed annually.[2] In Maranhão there is an incidence of 72 cases per 100,000 live births (1:1389) for SCD with one carrier of the sickle cell trait in every 30 births.[2]

In recent years, in countries like the USA, there has been a significant improvement in the survival of SCD patients. In 1973, the estimated mean age at death of SCD patients in the USA was 14.3 years, with 50% of deaths occurring during the first five years of life.[3] In 1992, a study in the USA showed that the mean age at death had increased to 42 years for men and to 48 years for women. In this study, the pattern of mortality varied with age and there was a peak incidence of death among SCD children occurring between one and three years of age; deaths of under 20-year-old patients were predominantly due to pneumococcal sepsis.[4]

Measures such as neonatal screening, the use of prophylactic penicillin between three months and five years of age, vaccination for pneumococcus, meningococcus and Haemophilus, and training in respect to early recognition of splenic sequestration, reduced the mortality rate to less than 5% in the first five years of life.[5] The authors concluded that these measures resulted in, on average, over 85% of affected children surviving beyond the age of 20.[5]

In Brazil, research on hemoglobinopathies, in particular sickle cell anemia, occurred after the government Ordinance No. 822 came into force on June 6, 2001; this law was designed to improve early diagnosis and to provide adequate treatment within the first few months of life. In December 2002, a test to diagnose hemoglobinopathies was implanted in the state of Maranhão.[6] The test was performed by the Association of Parents and Friends of Exceptional Children (APAE) in the city of São Luís, and by 2005 it was applied to 72% of all live births in the state.[6]

The objective of the current study was to compare trends in the mortality and hospital admission rates of SCD patients in Maranhão before and after the implementation of the neonatal screening test.

Methods

Data related to the deaths and hospitalizations of SCD patients in Maranhão from 1999 to 2012 were collected. Data related to the hospitalizations were obtained from an abbreviated version of the Hospital Information System (SIH) of the Brazilian National Health Service (SUS) annual database and data related to deaths were obtained from the Death Information System (SIM/SUS). The cases were selected using the 10th revision of the International Classification of Diseases (ICD-10) codes for SCD: D57.0 (SCD with crisis), D57.1 (SCD without crisis), D57.2 (double heterozygous sickle cell disorders) and D57.8 (other sickle cell disorders). Two age groups were determined: 0–19 years and 20 years or more. The period 1999–2005 was considered the pre-screening test implementation period and 2006–2012 was considered the post-implementation period. Although the test officially started in Maranhão in December 2002, it actually achieved true coverage from 2005 onwards. The rates of hospitalization and mortality due to SCD were calculated per 100,000 inhabitants. The total population served as the denominator because in Maranhão Black people make up 74% of the population and this methodology has already been reported in the literature and will allow comparisons between the results of this study and others.[7,8] The annual population data were obtained from the Brazilian Institute of Geography and Statistics (2000, 2010 and population estimates) and the total population of Maranhão grew from 5,418,354 to 6,714,314 between 1999 and 2012.

The rates of hospitalization and mortality due to SCD were calculated according to the following formula:

Mortality rate

$$= \left(\frac{\text{no of deaths due to sickle cell disease}}{\text{population}} \times 100,000 \right)$$

Hospitalization rate

$$= \left(\frac{\text{no of hospitalizations}}{\text{total resident population in year}} \times 100,000 \right)$$

Fisher's exact test was used to compare the percentage distribution of individuals by gender and age between the two periods. The non-parametric Kruskal–Wallis test was used to compare the median age between the periods.

To analyze the trend, a model of the evolution of the results in the initial period was created using multiple regression to check linear and quadratic models, with and without exponential growth, and the model that best fit the data was used. After analyzing the trends, R^2 values, and the results of the adjustments of regression analysis, a simple linear trend model was used to analyze the mortality and hospitalization rates. Extrapolation was subsequently performed for the first period, which would be the 'natural' trend. The effect of the 'natural' trend was then removed (detrended) for both periods and the means of the two periods were compared using the *t*-test for two groups. A value of significance of 0.05, which corresponds to a confidence level of 95%, was assumed for statistical analysis.

Results

Hospitalization rates

Totals of 128 and 840 SCD patients were hospitalized in the pre-test (before 2005) and post-test periods, respectively.

The median ages by year at admission ranged from eight to 35 years old. When the results of the two periods were compared, the median fell from 11.4 years in the pre-test period to 8.7 years in the post-test period (p-value = 0.0002 – Kruskal–Wallis).