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Newborn screening for sickle cell diseases in the United States: A review of data spanning 2 decades

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ABSTRACT

Sickle cell disease is a group of disorders, the majority of which are detected through state newborn screening programs. There is limited knowledge of disease prevalence in the U.S. population. We report 20 years of case finding and laboratory data for sickle cell disease and trait to assist in: planning for health services delivery; providing data for researchers; aiding in tracking health outcome trends; and assessing sickle gene prevalence in the newborn population. During the 20-year period, there were 39,422 confirmed cases of sickle cell disease among 76,527,627 newborn births screened (1:1941) and 1,107,875 laboratory reports of probable sickle trait among 73,951,175 newborn births screened (1:67). The highest sickle cell disease incidence during the 20 years was in the District of Columbia (1:437) followed by Mississippi (1:683) and South Carolina (1:771). For sickle cell trait, the highest incidences were in the District of Columbia (1:22), Mississippi (1:26), and South Carolina (1:31).

Background/introduction

Sickle cell disease (SCD) is one of the first-studied groups of genetic hemoglobinopathies of humans. The majority of individuals with SCD in the U.S. are detected through state newborn bloodspot screening (NBS) programs. The history and status of NBS for hemoglobinopathies in the U.S. have been previously reported in this journal.[1] Briefly, whole blood testing methods for hemoglobinopathies were applied to dried blood spots as a consequence of Guthrie's earlier work, and published in the early 1970s.[2] Following the lead of New York's NBS program,[3] other states (including the District of Columbia) gradually began to add NBS for sickle cell anemia (Hb SS), the most prevalent of the SCD.

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The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Health Resources and Services Administration, the American College of Medical Genetics, Emory University Medical School, or the University of Texas Health Science Center at San Antonio.

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Responding to research findings unequivocally demonstrating that penicillin prophylaxis could prevent infectious deaths from Hb SS,[4] a National Institutes of Health (NIH) Consensus Conference in 1987 recommended that, "… universal screening should be provided. State law should mandate the availability of these services while permitting parental refusal." They also addressed laboratory quality (which at the time included multiple small volume laboratories in some states) by noting that, "Centralization of laboratory services improves efficiency and decreases the probability of error."[5]

The Health Resources and Services Administration (HRSA), utilizing funds transferred from the NIH for this purpose, and the Centers for Disease Control and Prevention (CDC), through their evolving laboratory quality assurance program, provided funding and technical support, respectively, as state NBS programs began to add screening for Hb SS to their screening panels.[1,6] The last state to adopt universal NBS—New Hampshire—did so in 2006. Since the laboratory methodologies used for Hb SS screening have the ability to detect other hemoglobinopathies, many programs expanded their screening panel definitions beyond Hb SS to include other SCD. The Recommended Uniform Screening Panel (RUSP)[7] for U.S. newborns includes SCD as a core recommendation, including: (1) Hb SS; (2) sickle cell hemoglobin C disease (Hb SC); and (3) sickle beta thalassemia (Hb Sβ thal). All other hemoglobin variants are combined as a secondary target. (*Note*: The RUSP includes Hb Sβ thal as a single condition rather than 2 separate conditions, Hb $S\beta^+$ thal and Hb $S\beta^0$ thal.)

Individuals with SCD may have many acute and chronic complications, including anemia, severe infections, recurrent pain episodes, and chronic organ damage. Additionally, the high risk of infection and splenic sequestration are recognized as preventable causes of mortality and morbidity in young children. The ability to treat screen positive infants prophylactically with penicillin and prompt management of fever and splenic sequestration reduce mortality providing a sound justification for screening newborns for SCD. In spite of being one of the first genetic diseases identified, there is little understanding of SCD prevalence in the population; and little data on the quality and types of care individuals with SCD receive in the U.S. Additionally, there are no published comprehensive data defining the actual incidence of SCD in the U.S.

To plan resource allocation for health services delivery, to support research on SCD by providing an essential data resource for researchers, and for tracking trends in health outcome, we report the tabulation of 20 years of state case finding data for SCDs detected and diagnosed as a result of NBS. Further, we provide data on reported screening findings on individuals with sickle cell trait (Hb AS). As examples of how these data may be used, we also provide tabulations of SCD and Hb AS incidences over the study period. As the U.S. health care system changes, we anticipate that, among other uses, these data will be critical for determining the population to be served and assessing the adequacy of programs and policies that meet the public health and health care service needs of these individuals and their families.

Methods

Data collection

HRSA developed the National Newborn Screening and Genetics Resource Center (NNSGRC) in 1999, including a national NBS data collection system as a NNSGRC responsibility. The NNSGRC data collection effort built on the national NBS data collection and reporting protocols developed in the late 1980s by the Council of Regional Networks for Genetic Services (CORN), also with HRSA funding. The NNSGRC maintained these data online and available to the public from 2000 until 2012, when HRSA ceased funding the NNSGRC (2011 and 2012 data were not considered final at that time). Beginning in 1989 until 2012, all U.S. NBS programs except New York voluntarily contributed case finding and other performance evaluation information to a national dataset, maintained first by CORN and then by the NNSGRC.[8] New York data were maintained on a state-supported website[9] and periodically copied into the NNSIS to complete the national dataset. Developed primarily as a quality improvement tool, data elements were developed through a consensus process that included HRSA and CDC staff and a broad cross section of laboratory and non-laboratory personnel (including clinicians) working in NBS systems. The online data were part of a commercially developed National Newborn Screening Information System (NNSIS).

Originally, the CORN national NBS data were collected from each NBS program in questionnaire format. National NBS data reports were prepared from the data submitted and reviewed for accuracy by state program personnel before their final release. Moving to a secure online reporting system allowed generation of both preformatted and customized reports based on the submitted data, and annual reviews were discontinued. Data were considered to be final approximately 9 months following the end of a year, and further changes were allowed only in special circumstances (change in diagnosis). While these data were collected primarily for inter- and intra-program assessments and cover a limited time period, this dataset currently represents the only comprehensive national NBS data available, and NBS data have not been collected nationally since 2012.

Data validation

The 20 years of data tabulated and reported here represent data that were collected, summarized, and validated by each NBS program first at the end of 2000 (first decade data) and again prior to discontinuation of NNSGRC data collection activities in 2012 (second decade data). Because most NBS programs did not have a comprehensive data management system to import, transfer, report, and archive data, multiple sources and methods of data collection and reporting were used. The NNSIS system limited NBS data input to program-designated laboratory and follow-up personnel. Data accuracy was a program responsibility, and data correction capabilities were a part of NNSIS systems operation. In order to maintain the highest quality of available data, NNSGRC staff revalidated the tabulated data at the end of each decade.