Improved Survival Among Children with Spina Bifida in the United States

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Objective To evaluate trends in survival among children with spina bifida by race/ethnicity and possible prognostic factors in 10 regions of the United States.

Study design A retrospective cohort study was conducted of 5165 infants with spina bifida born during 1979-2003, identified by 10 birth defects registries in the United States. Survival probabilities and adjusted hazard ratios were estimated for race/ethnicity and other characteristics using the Cox proportional hazard model.

Results During the study period, the 1-year survival probability among infants with spina bifida showed improvements for whites (from 88% to 96%), blacks (from 79% to 88%), and Hispanics (from 88% to 93%). The impact of race/ethnicity on survival varied by birth weight, which was the strongest predictor of survival through age 8. There was little racial/ethnic variation in survival among children born of very low birth weight. Among children born of low birth weight, the increased risk of mortality to Hispanics was approximately 4-6 times that of whites. The black-white disparity was greatest among children born of normal birth weight. Congenital heart defects did not affect the risk of mortality among very low birth weight children but increased the risk of mortality 4-fold among children born of normal birth weight.

Conclusions The survival of infants born with spina bifida has improved; however, improvements in survival varied by race/ethnicity, and blacks and Hispanics continued to have poorer survival than whites in the most recent birth cohort from 1998-2002. Further studies are warranted to elucidate possible reasons for the observed differences in survival. *(J Pediatr 2012;161:1132-37)*.

Spina bifida, the most common type of neural tube defect, is defined as a protrusion of the spinal cord and/or meninges through a defect in the vertebral arches.[1-5] Although the birth prevalence of spina bifida significantly decreased after the introduction of mandatory fortification of enriched grain products with folic acid in the United States,[6-10] the population burden of spina bifida continues both in birth prevalence and in disparities in long-term outcomes. A birth prevalence estimate of spina bifida from 11 population-based surveillance programs in the United States was reported as 3.7 per 10 000 live births (1999-2001).[11] A 1-year survival estimate of 92.1% was reported by a study of 16 US birth defect monitoring programs for 1995-2001.[12] A recent long-term follow-up study of children with spina bifida in the United Kingdom estimated the survival experience at 1, 5, and 20 years of age to be 71%, 69%, and 66%, respectively.[13] Furthermore, another United Kingdom study found that the 5-year survival varied considerably by severity of the lesion, with a 40% lower survival among children with open lesions compared with those with closed lesions.[14]

Of particular concern is an observation of a lower survival experience among non-Hispanic black children born with spina bifida than among non-Hispanic white children born with spina bifida in the metropolitan Atlanta area.[15] Although the reasons for this racial/ethnic disparity in survival for children with spina bifida are unknown, this observation raises questions as to whether this finding might be evident in a national sample of children with spina bifida. As timely access to quality health care is important in reducing morbidity and mortality associated with spina bifida, it becomes important from a public health perspective to identify high-risk subpopulations of children with spina bifida, for whom targeted interventions may be made available to prevent complications and thereby improve their survival. In this study, we evaluated the long-term trend in survival among infants born with spina bifida by race/ethnicity and investigated maternal and infant characteristics associated with survival experience using data from 10 population-based surveillance programs in the United

AR	Arkansas	NY	New York
BPA	British Paediatric Association	OK	Oklahoma
CA	California	TX	Texas
CO	Colorado	UT	Utah
GA	Georgia	ICD-9-CM	*International Classification of Diseases, Ninth Revision, Clinical Modification*
IA	Iowa		
NC	North Carolina		

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States. We also examined variations in survival probability by race/ethnicity after adjusting for other factors.

Methods

A total of 5165 infants born with spina bifida were identified through 10 population-based birth defect monitoring programs located in the following regions: Arkansas (AR) birth cohort from 1993 to 2002; Georgia (GA) births in 5 central Atlanta counties from 1979 to 2003; California (CA) births in 11 counties from 1983 to 2002; Colorado (CO) births from 1989 to 2003; Iowa (IA) births from 1983 to 2003; North Carolina (NC) births from 1989 to 2003; New York (NY) births (excluding New York City) from 1983 to 2003; Oklahoma (OK) births from 1994 to 2003; Texas (TX) births from 1996 to 2003; and Utah births (UT) from 1994-2003 (**Table I**; available at www.jpeds.com). We included live-born infants with spina bifida (*International Classification of Diseases, Ninth Revision, Clinical Modification* [ICD-9-CM] codes 741.0 and 741.9) but excluded those with anencephaly (ICD-9-CM code 740.0), as well as those coded as possible/probable spina bifida cases based on the British Paediatric Association (BPA) codes modified by the Centers for Disease Control and Prevention. A previous report estimated the prevalence among older ages using a subgroup (n = 3390) of this study population that included those alive in 2002.[16]

Deaths among affected infants were ascertained by linking state vital records, medical records, and the National Death Index, and deaths were ascertained only from medical records and the National Death Index for 1998 data in CA. Patients without death records were considered alive at the end of the state's follow-up period and treated as censored in the survival analysis. Details about the regional surveillance programs have been published.[17]

Long-Term Trends in Survival Probability of Infants with Spina Bifida

To examine the temporal trends in survival probabilities over the 20-year study period, we compared survival probabilities to 1 year for each birth cohort (1983-1987, 1988-1992, 1993-1997, 1998-2003) overall and by race/ethnicity (non-Hispanic whites [referred to as whites], non-Hispanic blacks [referred to as blacks], Hispanics, and other). Trends in 1-year mortality were examined using data from 4 regions (GA, CA, IA, and NY) with at least 20 years of long-term follow-up. We calculated *P* values to show the significant increasing trends in 1-year survival over 4 birth cohorts.

Prognostic Factors of Survival Probabilities

Maternal and infant characteristics were obtained from medical records and birth certificates. Maternal characteristics considered were maternal race/ethnicity (white, black, Hispanic, other) and maternal age (<35 years vs ≥35 years). Infant characteristics included sex (male vs female), birth weight (<1500 g, 1500-2499 g, ≥2500 g), plurality (multiple vs singleton), presence of major heart defects (yes vs no), and spina bifida lesion level (cervicothoracic vs lumbosacral). We classified infants as having a major congenital heart defect using an algorithm we developed based on ICD-9/BPA classification codes. With the exception of NC, where only 4-digit ICD-9 codes were used, all regions used the most detailed ICD-9-CM or modified BPA codes. Codes for normal physiological findings in newborns or premature infants (eg, patent foramen ovale, patent ductus arteriosus), minor conditions such as tricuspid insufficiency, or unconfirmed cardiac defects were not considered structural heart defects. For heart defect codes that lacked specificity or may have included both major and minor cardiac defects, an expert in pediatric cardiology assisted in the decision for inclusion in the major heart defect group. The distribution of each characteristic by region is presented in **Table II** (available at www.jpeds.com).

One-Year Survival Probabilities for Infants with Spina Bifida by Selected Characteristics

For children born during 1997 to 2003 (n = 2259), Kaplan-Meier 1-year survival probabilities were estimated and Greenwood's method was used to calculate the variance and their 95% CIs.[18] The log-rank test was used to determine whether 1-year survival functions were significantly different among different levels of maternal and infant characteristics.[19] Adjusted hazard ratios were estimated using Cox proportional hazard models, stratified by survival time (1 month, 1 year, 5 years, and 8 years, which is the maximum years of follow-up for the limited cohort).[20] The assumption of proportionality was checked by plotting the estimated log-cumulative hazard versus the log of survival time to examine if they were parallel for different categories of the risk factors. Possible time-dependent trends were also tested to check the assumption of proportionality. Possible interactions between the significant unadjusted risk factors were also examined. Computations were performed using SAS-PC (version 9.13; SAS Institute, Cary, North Carolina).

Results

The cohorts of children with spina bifida from the 10 regions varied in size, birth years, follow-up years, and length of follow-up, with some data available representing birth years from 1979 to 2003 (**Table I**). The maternal and child characteristics of each regional cohort are shown in **Table II**. Although maternal white was the predominant racial/ethnic group for all regions combined, the relative proportions of blacks and Hispanics varied among regions. Infants of Hispanic mothers comprised >50% of the spina bifida cohorts in CA and TX, and infants of black mothers comprised >20% of the spina bifida cohorts in GA and NC. The proportion of mothers 35 years or older was similar across regions. For maternal education, there was a fair amount of variation in the proportion of children with spina bifida, with missing information for some regions (ie, GA and CA). There were no major regional