Contributions to Racial Disparity in Mortality among Children with Down Syndrome

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Objective To evaluate whether racial differences across a variety of medical factors collected in a longitudinal clinical database at a specialty clinical for children with Down syndrome provide insight into contributors to racial disparity in mortality.

Study design Comprehensive medical histories of 763 children receiving medical care at a Down syndrome specialty clinic were retrospectively reviewed regarding prenatal, postnatal, and medical issues, as well as subspecialty referrals. Frequency calculations and logistic regression were performed. The National Death Index was used to query death record databases to correlate medical histories with mortality data.

Results Prenatal drug use and intubation were significantly more frequent, but hyperbilirubinemia was significantly less frequent, in black children compared with white children with Down syndrome. Among children with Down syndrome aged <5 years, significant increases in referral to cardiology were seen for black children compared with white children. Trends were seen in an increased incidence of congenital heart disease for black children. Correlations with death records did not demonstrate differences in rates of cardiac-related deaths. Minimal racial disparity was seen for all other measures investigated.

Conclusion Racial disparity in mortality exists, but the underlying cause remains unidentified despite use of a comprehensive, longitudinal database of individuals with Down syndrome and review of death records. Referrals to cardiology might be a clue to the underlying cause, perhaps as an indicator of access to care, but cardiac disease does not account for the disparity in mortality. *(J Pediatr 2016;174:240-6)*.

An estimated 6037 infants with Down syndrome are born in the US annually, for an incidence of 1 in 691 live births.[1] Down syndrome has associated malformations and medical complications, including a high frequency of congenital heart disease (CHD) and risk for gastrointestinal malformations, leukemia, and obstructive sleep apnea.[2] The presence of CHD increases the need for hospitalization in children with Down syndrome.[3] The life course of individuals with Down syndrome is changing, with a significant increase in life expectancy noted over the last several decades.[4] Multiple factors have been studied to elucidate the etiology of this dramatic increase in life expectancy. The impact of earlier identification and improved treatment outcomes for CHD contributes significantly, but this does not fully account for the improved mortality.[5,6] Psychosocial factors, such as residence in a family or nonfamily setting, do not account for the differences in mortality.[7] The underlying etiology for improvement in the life expectancy of individuals with Down syndrome is not completely understood.

An investigation of changes in mortality through a 1983-1997 review of 17 958 individuals with Down syndrome found a significant racial disparity in life expectancy.[4] The median age at death differed by race: approximately 50 years for whites, 25 years for African Americans, and 10 years for other races.[4] These differences persist even after accounting for the presence of CHD.[8,9] The racial disparity in survival begins in infancy and persists into childhood.[9-11] Socioeconomic factors show racial disparities; compared with white mothers of infants with Down syndrome, black mothers are younger and more likely to be at a lower socioeconomic level.[12] Mortality studies in infants with Down syndrome do not show any associations between increased infant mortality and maternal age, education, race, or marital status, however.[13]

Survival is increasing in individuals with Down syndrome of all races, but African-American children with Down syndrome are showing comparatively less improvement in mortality.[9] Although some degree of difference in life expectancy by race is seen among the US population as a whole, the magnitude of this racial disparity is larger in the Down syndrome population.[14]

We sought to explore whether racial differences in a variety of medical factors collected in a longitudinal clinical database of children with Down syndrome provide insight into the underlying cause of the racial disparity in mortality. Spe-

CHD	Congenital heart disease
NDI	National Death Index

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cifically, we investigated factors that reflect the severity of illness, including prenatal, postnatal, and medical issues, and referrals to subspecialty providers as a gauge of access to care. To correlate racial disparities in these factors with mortality data, we searched national death record databases.

Methods

Institutional Review Board approval was obtained for the creation of a prospective research database in which participants were recruited from a Down syndrome clinic within the Division of Developmental and Behavioral Pediatrics at Cincinnati Children's Hospital Medical Center, a large pediatric academic medical center. Data were collected between 1984 and 2009 and included history information obtained during the course of routine medical visits and review of medical records. Medical histories of 827 individuals with Down syndrome aged ≤21 years were obtained.

History data were obtained by a review of medical records and parent reports; any discrepancies found were discussed with parents to achieve consensus. Forms were updated at each subsequent visit by the primary physician. Referrals for further evaluation were also recorded at each visit. A retrospective review with attention to racial disparities was performed.

The mean age at the first visit was documented and referred to the subject's initial visit to the subspecialty Down syndrome clinic. Cases with mosaic Down syndrome were excluded from this analysis (n = 14), because the mortality rate is lower in these children compared with children with nonmosaic Down syndrome,[15] and because no children with mosaic Down syndrome in the study population were black/African-American. Race was determined from parent report and the electronic medical record; to maintain consistency, the selections available in the electronic medical record are used in this report; black/African American is referred to as "black" (coded as 0) and white/Caucasian, as "white" (coded as 1). Race was unavailable for 7 individuals. An additional 43 individuals identified as American Indian, Asian, Pacific Islander, or other race were excluded from the analysis owing to insufficient sample sizes for analysis. The remaining 763 individuals are the focus of this study. ZIP code of residence was recorded at initial enrollment and updated with changes in address, but these were not tracked in our database; only the most recent ZIP code was recorded in our database. Median household income was derived from home ZIP code, if available, using US Census data.[16,17]

The birth history information collected included parent-reported prenatal and postnatal issues, which were scored as either present or absent and included maternal smoking, drug and alcohol use, preterm labor, polyhydramnios, toxemia, hyperemesis, gestational diabetes, hypoglycemia, bleeding, cesarean delivery, breech delivery, multiple births, in vitro fertilization, oxygen requirement, neonatal intensive care unit admission, respiratory distress, thrombocytopenia, pulmonary hypertension, feeding problems, leukemoid reaction, hyperbilirubinemia, polycythemia, meconium aspiration, temperature control, requirement for continuous positive airway pressure, and neonatal seizures. Sum variables were created to provide an overall rating of the total number of prenatal or postnatal risk factors for each child with Down syndrome.

The medical history detailed the presence/absence of various medical conditions, including any CHD, gastrointestinal malformation, ophthalmologic disease, otolaryngology concerns, autoimmune and thyroid conditions, atlantoaxial instability, seizures, sleep apnea, and other conditions. Sum variables were created to provide an overall rating of the total number of medical complications for each child. Medical history data were confirmed through hospital medical records. Frequency of visits and referrals made to other medical providers (eg, cardiology, genetics, gastroenterology, neurology, ophthalmology, orthopedics, otolaryngology, pulmonary) and allied health (eg, audiology, feeding, occupational therapy, psychology, speech) were collected as well. Evaluation by any of these medical providers before the visit to the Down syndrome clinic was noted.

Data Analyses

To explore potential racial disparities in medical issues, logistic regression was used to predict race from the sum of 4 different counts: prenatal risk factors, postnatal risk factors, medical conditions, and referrals. Five additional logistic regressions were conducted to explore potential differences in race predicted from the presence of specific prenatal, postnatal, and medical issues as well as specific medical and allied health referral patterns. Prenatal, postnatal, medical issues, and referrals were included in the models if they occurred with >0% frequency in the sample.

Because the majority of subjects were aged <5 years, subanalyses were performed for this age group. These analyses were performed to distinguish deaths occurring early in childhood, because these would be more likely to reflect changes in CHD, and because the rate of death before age 5 years has decreased over time.[4,5] Final medical histories for these children aged <5 years were obtained primarily in the 2000s (60.4%), with 26.5% obtained in the 1990s and 13.1% obtained in the 1980s. Given the changes in care of individuals with Down syndrome over the past several decades, a subanalysis by decade of original clinical evaluation was also performed to investigate the impact of time on selected variables.[4]

The National Death Index (NDI) is a centralized database of death record information maintained in state vital statistics offices through the Center for Disease Control and Prevention.[18] Working with these state offices, the National Center for Health Statistics established the NDI as a resource to aid epidemiologists and other health and medical investigators with mortality ascertainment activities. The NDI has been shown to have high sensitivity for use in research.[19] The NDI was searched to identify subjects in the clinical database who had existing death records and were deceased. Patient information was provided to NDI staff to review the