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Racial Differences by Gestational Age in Neonatal Deaths Attributable to Congenital Heart Defects—United States, 2003-2006

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1 figure, 2 tables omitted

CONGENITAL HEART DEFECTS ARE DIAGnosed in approximately 1% of births in the United States[1] and account for the largest proportion of infant mortality attributable to birth defects.[2] Congenital heart defects are multifactorial in origin and have several recognized genetic causes (e.g., DiGeorge and Williams-Beuren syndromes)[3] and noninherited risk factors (e.g., maternal pregestational diabetes and rubella infection).[4] Approximately 70% of infant deaths attributable to congenital heart defects occur neonatally (age <28 days).[5] U.S. studies have shown that all-cause neonatal mortality rates are higher among term infants of black mothers compared with white mothers, but lower among preterm infants of black mothers compared with white mothers.[6,7] To assess neonatal mortality attributable to congenital heart defects by maternal race and gestational age, CDC analyzed linked U.S. birth and infant death data for 2003-2006. This report summarizes the results of that analysis, which found that 4.2% of all neonatal deaths and 24.5% of neonatal deaths attributable to birth defects had a congenital heart defect noted as the underlying cause. Among preterm births (<37 completed weeks' gestation), neonatal mortality rates attributable to congenital heart defects were lower for blacks (4.5 per 10,000 live births) compared with whites (6.8). However, among term births (≥37 completed weeks' gestation), neonatal mortality rates attributable to congenital heart defects were higher for blacks (1.5 per 10,000 live births) than for whites (1.3). The reasons for these racial differences by gestational age are unclear and will require further examination, including assessment of differences in prenatal diagnosis and prevalence at birth of congenital heart defects, and reporting of causes of death.

This analysis used 2003-2006 linked* birth/infant death data, the most recent available.† Included were records of all neonates (aged <28 days) whose underlying cause of death on the death certificate was classified as a congenital heart defect according to the *International Classification of Diseases, 10th Revision*, with codes Q20.0–Q26.9 (excluding Q21.1, persistent foramen ovale‡ and Q25.0, patent ductus arteriosus, because these are considered normal conditions of prematurity). The analysis was restricted to infants of white and black mothers as reported on the birth certificate; those of Hispanic ethnicity and other racial/ethnic groups were excluded. Linked records with a missing gestational age (0.6% of the total), those with implausible gestational ages based on Alexander's index of birth weight for gestational age norms (0.6%),[6] and those with gestational ages <20 weeks or >44 weeks (1.1%) were excluded.

Because not all infant death records could be linked to the corresponding birth certificate, estimates of neonatal deaths were weighted according to the percentage of records linked by state and age at death. Poisson regression was used to calculate the rate ratio (RR) comparing neonatal mortality attributable to congenital heart defects among infants of black mothers with white mothers by gestational age group. Congenital heart defect neonatal mortality rates by weeks of gestational age also were estimated for infants of black mothers compared with white mothers.

The analysis included 11,383,665 live births in the United States during 2003-2006. Overall, of 54,008 neonatal deaths, 2,256 (4.2%) had a congenital heart defect noted as the underlying cause, including 1,777 (5.4%) of 33,205 infants of white mothers and 479 (2.3%) of 20,803 infants of black mothers. Deaths attributable to congenital heart defects were 24.5% of all neonatal deaths attributable to birth defects. The neonatal mortality rate attributable to congenital heart defects was 2.0 per 10,000 live births. Hypoplastic left heart syndrome was the most commonly specified congenital heart defect—related underlying cause of neonatal death for infants of white (480 [27%]) and black (126 [26%]) mothers; 38% of the deaths were listed as "congenital malformation of heart, unspecified." A significantly lower proportion of neonatal deaths with transposition of the great arteries as the underlying cause occurred in infants of black mothers (2%) compared with white mothers (6%), but a significantly higher proportion of neonatal deaths caused by pulmonary atresia occurred in infants of black mothers (3%) compared with white mothers (2%).

Preterm infants (born at <37 weeks' gestation) accounted for 18% of the 2,312,080 births to black mothers and 11% of the 9,071,585 births to white mothers. Neonatal mortality rates attributable to congenital heart defects varied by week of gestation and maternal race. Overall, neonatal mortality rates attributable to congenital heart defects were not significantly different when comparing infants of black mothers (2.1 per 10,000 live births) with infants of white mothers (2.0) (Rate ratio [RR] = 1.1; p = 0.28). However, the neonatal mortality rate attributable to congenital heart defects among preterm infants of black mothers (4.5 per 10,000) was significantly lower than

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that for preterm infants of white mothers (6.8) (RR=0.7; p<0.001). In contrast, among infants delivered at 37-44 weeks, the neonatal mortality rate attributable to congenital heart defects among infants of black mothers (1.5 per 10,000) was higher than the neonatal mortality rate among infants of white mothers (1.3) (RR=1.2; p=0.03).

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CDC Editorial Note: The findings in this report indicate that although the overall neonatal mortality rate from congenital heart defects does not differ significantly between infants born to white and black mothers, differences can be observed by gestational age group. Among term infants, the rate for neonatal mortality attributable to congenital heart defects was 20% higher among infants of black mothers compared with white mothers, but among preterm infants, the rate was 30% lower for infants of black mothers compared with white mothers. Similar patterns have been reported for all-cause neonatal mortality by gestational age group in the United States during 1989-2001.[7] Although reports of infant mortality attributable to any birth defect have indicated that infants born to black mothers had higher mortality rates than infants born to whites,[2,5] these studies did not analyze the differences by gestational age.

The reason for the lower rate of all-cause neonatal mortality among preterm infants of black mothers compared with white mothers is unclear. One possibility is that live-born infants who die shortly after birth might be misclassified as fetal deaths, particularly those born at early gestational ages.[7] The fetal mortality rate in the United States is approximately twice as high among blacks as among whites,[8] and differences by race in reporting fetal deaths versus early neonatal deaths might exist. Recent research has shown variation by state in classification of neonatal death at <24 hours versus fetal death for infants at the limits of viability (i.e., gestation of <24 weeks or birth weight <500 g).[9] Whether such variation might also occur by race is unknown.

Also unclear is whether factors specific to congenital heart defects contribute to the differences in black and white neonatal mortality patterns by gestational age. Potentially, differences in prevalence of specific types of congenital heart defects might explain the differences in mortality patterns; however, previous studies examining congenital heart defect prevalence have not identified many racial differences in specific types of congenital heart defects or in congenital heart defects overall.[1,10] Among studies that included birth defect prevalence among live births, stillbirths, and pregnancy terminations, no racial difference was observed for prevalence of hypoplastic left heart syndrome, the most common specific cause of death attributable to congenital heart defects.[1,10] Some data have shown that infants of black mothers have a lower prevalence of transposition of the great arteries[1,10] and coartaction of the aorta,[1] but a higher prevalence of tetralogy of Fallot[10] and pulmonary atresia/stenosis.[1]

The findings in this report are subject to at least three limitations. First, because of the large percentage of cases in which the underlying cause of death was unspecified, the results related to the distribution of specific causes should be interpreted with caution. Second, this analysis only included deaths with a congenital heart defect listed as the underlying cause; deaths were not included if congenital heart defects were instead classified as a contributing cause (e.g., Down syndrome as underlying with atrioventricular septal defect as contributing). However, such possible underestimation of deaths attributable to congenital heart defects would impact the analysis of racial differences only if differential reporting of the underlying cause of death occurred among racial groups. Finally, gestational age can be inaccurate on the birth certificate and might be less accurate among preterm births.[6] Although cases with implausible gestational age/birth weight combinations were excluded, this analysis might have included some misclassified gestational ages.

Adjusting for gestational age or its correlates (such as birth weight), as has been done in some previous studies, obscures the differences in neonatal mortality rates by gestational age, and thus should be avoided. Efforts to reduce neonatal mortality rates attributable to congenital heart defects should include strategies to decrease mortality among infants with congenital heart defects through timely and appropriate medical and surgical treatment and to prevent the occurrence of congenital heart defects, where possible, by addressing modifiable potential risk factors such as pregestational diabetes, obesity, and maternal smoking.[4] The role of gestational age in differences in neonatal mortality among infants born to white and black mothers is unclear and requires further investigation, in-

What is already known on this topic?

Congenital heart defects are associated with preterm delivery and are the largest contributor to neonatal mortality attributable to birth defects.

What is added by this report?

Neonatal mortality attributable to congenital heart defects was 30% lower among preterm infants born to black mothers compared with preterm infants born to white mothers in the United States during 2003-2006; however, among term infants, those born to black mothers had 20% higher neonatal mortality attributable to congenital heart defects compared with those born to whites.

What are the implications for public health practice?

The reasons for racial differences by gestational age in neonatal mortality attributable to congenital heart defects are unclear and can only be understood through further examination, including assessment of differences in prenatal diagnosis, prevalence at birth of congenital heart defects, and reporting of causes of death.

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*Includes all infant deaths in a given year linked to their corresponding birth certificates, whether the birth occurred in that year or the previous year. Linkage completion by state ranged from 94% to 100%; a mean of 27 states linked 100% of their records each year.
†Available at http://www.cdc.gov/nchs/data_access/vitalstatsonline.htm.
‡Although Q21.1 includes atrial septal defects, most deaths coded to this category are persistent foramen ovale. For this reason, all Q21.1 deaths were excluded from the analysis.

Balamuthia mandrillaris Transmitted Through Organ Transplantation—Mississippi, 2009

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1 figure, 2 tables omitted

ON DECEMBER 14, 2009, A PHYSICIAN IN Mississippi contacted CDC to report possible transplant-transmitted encephalitis in two kidney transplant recipients who shared the same organ donor. Histopathologic testing of donor autopsy brain tissue at CDC showed amebae, and subsequent testing of specimens from the donor and the two kidney recipients confirmed transmission by transplantation of *Balamuthia* granulomatous amebic encephalitis (GAE), a rare disease caused by *Balamuthia mandrillaris*, a free-living ameba found in soil.[1] One kidney recipient, a woman aged 31 years, died; the other recipient, a man aged 27 years, survived with neurologic sequelae. Recipients of the heart and liver from the same donor received preemptive therapy and have shown no signs of infection. The donor, a previously healthy boy aged 4 years, was presumed to have died from acute disseminated encephalomyelitis (ADEM), an autoimmune neurologic disease, after infection with influenza A. An investigation was conducted by the state health departments in Mississippi, Kentucky, Florida, and Alabama and CDC to characterize the cases, elucidate possible exposures in the donor, and develop recommendations for early detection and prevention. This is the first reported transmission of *Balamuthia* by organ transplantation. Clinicians should be aware of *Balamuthia* infection as a potentially fatal cause of encephalitis. Organ procurement organizations (OPOs) and transplant centers should be aware of the potential for *Balamuthia* infection in donors with encephalitis of uncertain etiology, and OPOs should communicate this elevated risk for infection to transplant centers so they can make an informed risk assessment in the decision to accept an organ.

Organ Donor

The organ donor, a boy aged 4 years from Kentucky, was living with relatives in Mississippi in October 2009, when he developed a transient febrile illness. He was diagnosed with influenza A infection by rapid influenza test on October 25 and prescribed antivirals; his symptoms resolved without hospitalization. On November 3, the boy had sudden onset of headache and seizures and was hospitalized. Cerebrospinal fluid (CSF) demonstrated lymphocytic pleocytosis (170 white blood cells/mm^3) and normal protein (29 mg/dL); magnetic resonance imaging (MRI) of the brain showed numerous small enhancing lesions and edema. An extensive search for viral, bacterial, and fungal etiologies of encephalitis was unrevealing. His clinical presentation, CSF findings, and MRI were thought to be most consistent with a diagnosis of ADEM, an immune-mediated encephalitis that can follow influenza or other infections. He was treated symptomatically and discharged on November 6.

The boy was readmitted on November 10 with recurrent seizures. MRI of the brain demonstrated progression of several of the enhancing lesions; CSF again demonstrated lymphocytic pleocytosis (150 cells/mm^3) and normal protein (44 mg/dL). He was treated for presumed worsening ADEM with intravenous corticosteroids and immunoglobulin. He developed subarachnoid hemorrhage and brain stem herniation on November 18 and was pronounced brain dead the next day. His heart, liver, and kidneys were transplanted into four recipients at three different transplant centers on November 20. On December 16, histopathologic examination of the donor's brain tissue at CDC revealed the presence of abundant amebae morphologically suggestive of

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