

Omphalocele and Gastroschisis: Black-White Disparity in Infant Survival

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BACKGROUND: Racial/ethnic variations in the occurrence of abdominal wall defects have been previously noted but it remains poorly understood whether race/ethnicity is a determinant of survival among affected infants. **METHODS:** Study was conducted on cases of gastroschisis and omphalocele recorded for the years 1983–1999 at the New York Congenital Malformation Registry. Adjusted and unadjusted hazard ratios were generated from a Proportional Hazards Regression model to compare survival among affected Blacks, Hispanics and Whites. The major end point of analysis was differences in all cause mortality among infants with abdominal wall birth defects across different racial/ethnic groups. **RESULTS:** Among the three racial/ethnic groups, 1481 infants were diagnosed with either omphalocele (978 or 66%) or gastroschisis (503 or 34%). Overall infant mortality rate (IMR) was 182 per 1000, with 74% of the deaths occurring within the first 28 days of life. Omphalocele infants had significantly higher infant mortality (IMR = 215 per 1000) than infants with gastroschisis (IMR = 118 per 1000)[$p < 0.0001$]. Overall, Black infants with abdominal wall defects had lower mortality indices than Whites and Hispanics. However, when considered as separate disease entities, Black infants were twice as likely to survive as compared to Whites if they had omphalocele [Adjusted Hazard Ratio (AHR) = 0.52; 95% Confidence Interval (CI) = 0.37–0.74], and twice as likely to die as Whites if they had gastroschisis instead (AHR = 2.23; 95% CI = 1.16–4.28). For both defect subtypes, Hispanics have risks for infant mortality comparable to Whites. **CONCLUSIONS:** The natural history of omphalocele and gastroschisis co-varies with race. Black infants with gastroschisis have worse survival outcomes while those with omphalocele have better chances of survival than their White or Hispanic counterparts. *Birth Defects Research (Part A) 70:586–591, 2004.* © 2004 Wiley-Liss, Inc.

INTRODUCTION

Over the previous two decades, congenital malformations have remained the leading cause of infant demise, accounting for approximately 20% of all deaths occurring during the first year of life (Petrini et al., 2002). Race/ethnicity appears to be an important determinant of survival among babies affected with birth defects. Nationwide, it has been estimated that, on average, the birth defects infant mortality for Black infants was about 26% higher than that for Whites (Anderson, 2001). Another study conducted among Michigan children born with congenital anomalies found that the overall mortality rates for Black children were significantly higher than for Whites although the disparity vanished after controlling for other suspected confounding characteristics (Berger et al., 2003).

However, the aforementioned studies examined racial disparity in survival among all infants with birth defects, regardless of the nature of the malformation. The distinction is important because the natural history of birth de-

fects in relation to survival is different depending on the lethality of the malformation. Even in those cases where certain birth defects appear similar, it has been demonstrated that they may have different survival prognoses (e.g., omphalocele and gastroschisis) [Salihu et al., 2003; Forrester and Merz, 1999; Rankin et al., 1999]. Hence, it is important to have malformation-specific estimates for infant mortality when examining the role of race/ethnicity as a determinant of survival. This approach has the potential for providing useful information regarding malformations that exhibit significant levels of racial disparities in survival and those that do not, and would be helpful in devising effective intervention strategies to narrow racial/

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ethnic disparities among this highly vulnerable population of infants.

METHODS

The data for this study were obtained from the New York State Congenital Malformations Registry (NYCMR), one of the largest statewide, population-based birth defects registries in the nation. The NYCMR uses passive case ascertainment, relying on reports from hospitals and physicians. State regulations mandate all physicians and other hospital staff to report major congenital malformations at birth through the age of 2 years. New case reports are matched against existing registry data to eliminate duplication. For each case, reporting physicians, hospitals and genetics laboratories are asked to provide a narrative description of the congenital anomaly, and NYCMR staff review all such reports carefully. Incomplete reports and non-specific diagnoses are followed up with the reporting source.

Most NYCMR prevalences for major birth defects are similar to those of other registries that use active case-finding, such as the California Birth Defects Monitoring Program and the Metropolitan Atlanta Congenital Defects program (Druschel et al., 2001). The completeness of the NYCMR data has been found to be satisfactory by other investigators (Honein and Paulozzi, 1999).

Case Definition

We analyzed data covering the period 1983-1999 for all diagnosed cases of omphalocele and gastroschisis among live-born infants in the State of New York. Based on the diagnosis and narrative information provided by the reporting entity, the following case definitions were used to codify a case as gastroschisis or omphalocele:

- Gastroschisis was defined as an abdominal wall defect, located lateral to a normal umbilicus but not involving the umbilical ring. The herniated viscera are often covered by exudate but no membrane covers the loops of gut floating in amniotic fluid.
- Omphalocele was defined as midline abdominal wall defect limited to an open umbilical ring. The viscera herniate into the base of the umbilical cord and are covered by an amnioperitoneal membrane.

The primary outcome of interest was infant mortality, which was defined as death of the child before the first birthday. Information on infant survival was obtained through the routine linkage maintained by the Vital Statistics Records as required by the National Center for Health Statistics. We also conducted a limited analysis for neonatal (death of the infant within the first 28 days of life), early neonatal (death of the infant before the 7th day of life), late neonatal (death of the infant from between the 7th and the 28th day of life) and post-neonatal (death of the infant between the 28th and 365th day of life) mortality. We then compared these indices among Black, White and Hispanic infants. An infant was assigned to one of the three racial/ethnic groups based on the race/ethnicity of the mother. In this study, the designation of Black denotes Black, non-Hispanic, and similarly, White stands for White, non-Hispanic.

We compared the following socio-demographic characteristics and pregnancy history across the three racial/ethnic groups of interest: maternal age, parity, maternal education, place of residence, mode of delivery and level of

care. Maternal age was categorized into mothers aged < 25 and those \geq 25 years. Parity refers to the total number of live deliveries the mother had previously experienced, and was classified into primipara (\leq 1) and multipara (>1). Maternal education was divided into mothers with high school level of education and those with less than high school education. Place of residence was categorized as either living in New York City or outside New York City. Similarly, mode of delivery was either vaginal or C-section, and level of care refers to the facility where delivery of the child took place. The level of care was categorized into four classes (Level I-Level IV) in ascending level of sophistication. Level I represents facilities with the barest minimum of services, while Level IV represents the highest level that offers specialized surgery. If abdominal wall defect was the only anomaly in the infant then it was categorized as isolated, otherwise it was categorized as multiple. Infants with minor congenital anomalies (e.g., isolated polydactyly) or gastrointestinal anomalies associated with the ventral wall defect were classified as isolated (Calzolari et al., 1995).

Ethical Considerations

Before the commencement of analysis, approval was obtained from the New York State Department of Health Institutional Review Board.

Statistical Analysis

Analysis was conducted using SAS software (version 9.0, SAS Institute, Cary, NC). Infant mortality rates (IMR) among infants with omphalocele and gastroschisis were calculated by dividing counts of infant deaths by total number of live births within the period multiplied by 1000. Infant mortality among Blacks, Whites and Hispanics was compared using the Kaplan-Meier product-limit estimator, which calculated the cumulative probability of death for each racial/ethnic group. To determine whether the difference in infant mortality among the three racial/ethnic groups was significant, we applied the Wilcoxon statistic instead of the more common Mantel log-rank test because death counts, regardless of defect subtype, were more dense in the earlier part of the infancy period (neonatal) and became sparse post-neonatally. We used the Proportional Hazards Regression model to derive unadjusted and adjusted hazard ratios for infant mortality after testing for the non-violation of the proportionality assumption in each case. We confirmed this by plotting the log-negative-log of the Kaplan-Meier estimates of the survival function versus the log of time. The resulting curves were parallel. Adjusted hazard ratios were derived by loading all the variables considered as potential confounders into the model. All tests of hypothesis were two-tailed with a type 1 error rate set at 5%.

RESULTS

From 1983 to 1999, a total of 1524 neonates with either gastroschisis (514 or 33.7%) or omphalocele (1010 or 66.3%) were documented in the State of New York. All neonates with mothers recorded as White, Black or Hispanic were included in the study (n=1481). Half (50%) of all the abdominal wall defects were diagnosed among White non-Hispanics, 27% among Black non-Hispanics, 20% among Hispanics and 3% among other racial groups. A break-

Table 1
Selected Maternal Socio-Demographic and Pregnancy Characteristics Among White, Black and Hispanic Live Births with Omphalocele or Gastroschisis

	White, NH* (N = 758)		Black, NH* (N = 417)		Hispanic (N = 306)		#P-value
	n	%	n	%	n	%	
Mother's Age							<0.0001
Less than 25 years	345	(45.5)	221	(53.0)	192	(62.8)	
25 years and above	413	(54.5)	196	(47.0)	114	(37.2)	
Parity							0.03
Primipara	389	(51.3)	181	(43.4)	163	(53.3)	
Multipara	369	(48.7)	235	(56.4)	143	(46.7)	
Not stated	0	(0.0)	1	(0.2)	0	(0.0)	
Education							<0.0001
Less than high school	164	(21.7)	149	(35.7)	158	(51.6)	
High school and above	565	(74.5)	252	(60.4)	137	(44.8)	
Unknown	29	(3.8)	16	(3.9)	11	(3.6)	
Residence							<0.0001
New York City	96	(12.7)	279	(66.9)	247	(80.7)	
Outside New York City	662	(87.3)	138	(33.1)	59	(19.3)	
Delivery method							<0.0001
Vaginal	365	(48.2)	277	(66.4)	197	(64.4)	
C-section	349	(46.0)	130	(31.2)	100	(32.7)	
Unspecified	44	(5.8)	10	(2.4)	9	(2.9)	
Level of care							<0.0001
Level I	212	(28.0)	65	(15.6)	41	(13.4)	
Level II	40	(5.3)	31	(7.5)	11	(3.6)	
Level III	121	(16.0)	107	(25.7)	134	(43.8)	
Level IV	357	(47.0)	202	(48.3)	115	(37.6)	
Not specified	28	(3.7)	12	(2.9)	5	(1.6)	

*NH stand for non-Hispanic.

#P-values refer to comparison between non-missing groups, and were generated by means of the χ^2 test.

down of the racial distribution of gastroschisis and omphalocele showed variation by race. Among Blacks, the overwhelming majority of cases of the defects were omphalocele (81.5%), as compared to only 60% and 58.8% among Whites and Hispanics respectively ($p < 0.0001$).

Table 1 summarizes selected characteristics of these mothers. There were racial/ethnic differences in terms of all the considered variables. Most Hispanic (62.8%) and Black (53%) mothers were younger than 25 years of age, while the majority of Whites (54.5%) were older than 25 years. There was an equal proportion of primiparous and multiparous mothers overall, although Black mothers were more likely to be multiparous in comparison to Whites and Hispanics. An overwhelming majority of White mothers had achieved at least the level of high school education, in sharp contrast to Hispanic mothers among whom the majority did not attain high school. Black mothers fell in-between. About 56% of the mothers resided outside New York City, and the majority of them were White. In contrast to White mothers, most Black and Hispanic mothers resided in New York City. Among 66 cases (4.0%), the mode of delivery could not be determined or was not clearly stated. Among those with specified delivery method (96.0%), the predominant route was vaginal involving 862 cases (59%). Racial/ethnic differences were also apparent in this respect. When compared to Whites, Hispanic and Black mothers were more likely to undergo vaginal delivery of infants with abdominal wall defects.

About one-third of all infants with abdominal wall defects (32.8%) had additional anomalies (either structural or chromosomal). Although the proportion of multiple lesions tended to be higher among Blacks (35.7%) as compared to Whites (31.5%) or Hispanics (31.7%), these differences were not significant ($p = 0.30$). When these defects were examined separately, 38% of Black infants with omphalocele had extra malformations against 41.7% of Whites and 40.6% of Hispanics ($p = 0.7$). The result did not differ from that of gastroschisis infants, among whom 23.4% of Blacks, 16% of Whites and 19.1% of Hispanics had multiple anomalies ($p = 0.3$).

Out of the total 1481 infants with abdominal wall defects across the three racial/ethnic groups of interest in this study, 1479 (99.9%) had information concerning survival during the first 365 days of life, consisting of 502 cases of gastroschisis and 977 omphaloceles. The two excluded cases comprised one White omphalocele and a Black gastroschisis baby. Table 2 presents mortality among babies with abdominal wall defects within the first year of life. Overall, crude infant mortality rate was 182 per 1000, with 74% of the deaths occurring during the first 28 days of life. Omphalocele infants had significantly higher mortality (infant mortality rate = 215 per 1000) than gastroschisis infants (infant mortality rate = 118 per 1000)[$p < 0.0001$]. Table 2 reveals that mortality among infants with abdominal wall defects was lowest among Blacks, while Hispanics and Whites had comparable rates. However, since omphalocele differs significantly from gas-

Table 2
Mortality Among Infants with Omphalocele and Gastroschisis by Race/Ethnicity, New York State, 1983–1999

	White		Hispanic		Black		P-value
	Number	%	Number	%	Number	%	
Infant mortality	146	19.3	59	19.3	64	15.4	0.2
Neonatal mortality	114	15.1	45	14.7	40	9.6	0.03
Early	97	12.8	38	12.4	34	8.2	0.04
Late	17	2.2	7	2.3	6	1.4	0.6
Postneonatal mortality	32	4.2	14	4.6	24	5.8	0.4

trochsis in terms of survival probability, we separated the data into the two sub-groups, and stratified by race/ethnicity (Figures 1 and 2).

Figures 1 and 2 depict different prognoses for omphalocele and gastroschisis depending on the race/ethnicity of the individual. Among omphalocele babies, Blacks had the best prognosis for survival as compared to both Whites and Hispanics, the latter two having comparable survival probabilities. However, the reverse was the case among infants affected with gastroschisis. White and Hispanic infants with gastroschisis were significantly less likely to die in the first year of life than their Black counterparts. After controlling for potentially confounding factors of survival, Black infants were twice as likely to die if they had gastroschisis, but twice as likely to survive if they were to have omphalocele instead, as compared to Whites (Table 3). Again, the adjusted risk estimates of infant mortality for Hispanics and Whites were comparable regardless of the type of the defect.

DISCUSSION

This study found an infant mortality rate of 182 per 1000 for the combined abdominal wall defects, an estimate that is

comparable to the range of 95 to 186 per 1000 reported by other investigators (Lafferty et al., 1989; Salihu et al., 2003; Salihu et al., 2002; Forrester and Merz, 1999). The birth-defects-specific infant mortality rate for the State of New York was recently reported at 137.8 per 1000 (Petrini et al., 2002). The modest disparity between the overall birth defects-specific infant mortality rate (IMR) and the abdominal wall defects-specific IMR from our study is not unexpected since the former represents a composite value contributed by both very low and high mortality indices for minor and major anomalies respectively. As in previous studies (Salihu et al., 2003; Forrester and Merz, 1999; Torfs et al., 1990; Morrow et al., 1993; Tan et al., 1996; Carpenter et al., 1984; Martinez-Frias et al., 1984; Salihu et al., 2002) omphalocele infants had higher mortality higher rates than those with gastroschisis (215 per 1000 versus 118 per 1000). Irrespective of race/ethnicity, infants with omphalocele were more likely to have multiple anomalies than those with gastroschisis, a marker that is strongly associated with poor survival prognosis (Cleves et al., 2003) and explains the survival advantage of gastroschisis infants.

An important finding in this study is the variation in infant mortality for abdominal wall defects across racial

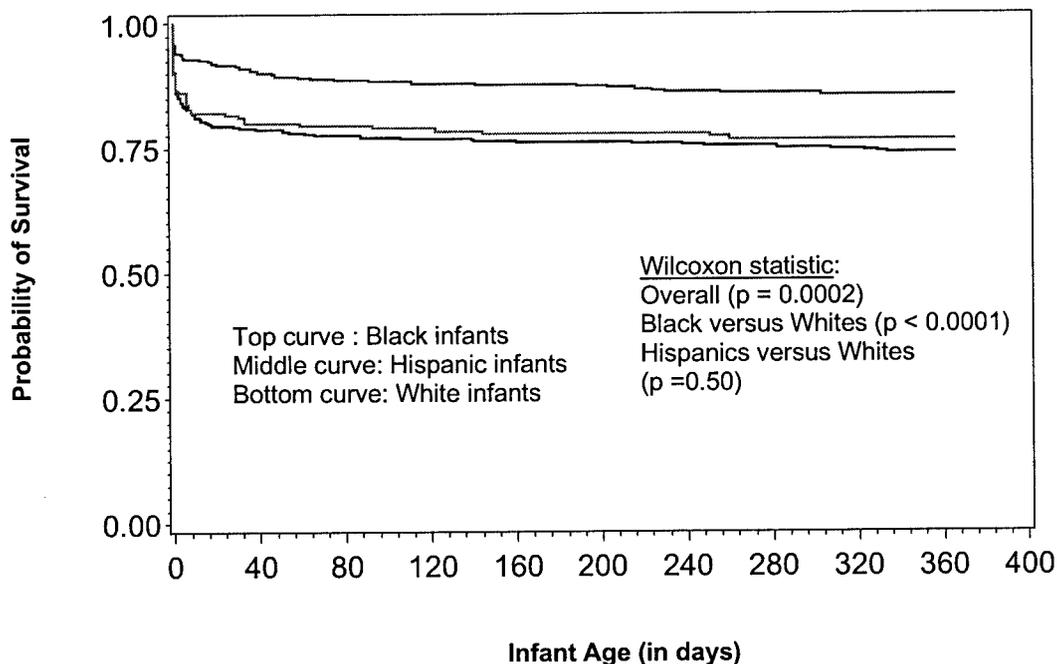


Figure 1. Kaplan-Meier survival curves for differences in infant mortality by race/ethnicity among infants with omphalocele

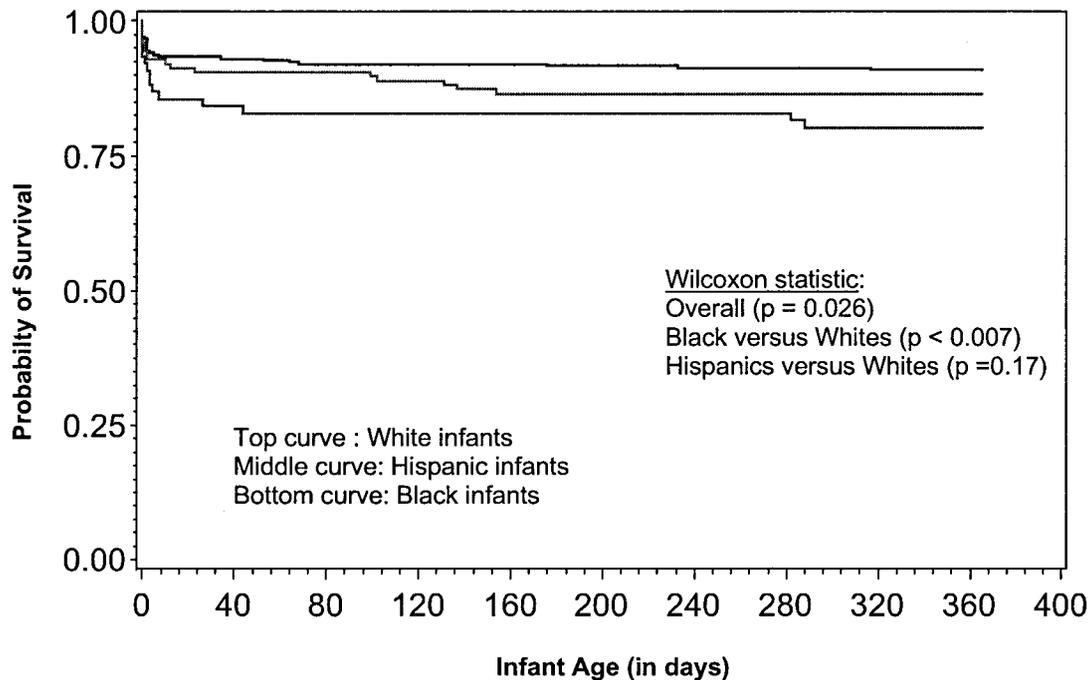


Figure 2. Kaplan-Meier survival curves for differences in infant mortality by race/ethnicity among infants with gastroschisis

groups. When examined as a group, Blacks with abdominal wall defects seemed to have a lower IMR than Whites and Hispanics (infant death rate for Blacks = 15.3% versus 19.3% for the other two groups). The national IMR due to birth defects is generally higher for Blacks (169.2 per 1000) than for Whites (134.4 per 1000) [Petrini et al., 2002]. However, other authors who have examined specific birth anomalies, like neural tube defects, have also reported better survival outcomes among Black infants as compared to Whites (Davidoff et al., 2002). Although this corresponds with our results, sub-analysis of our data revealed additional information that suggests caution in making generalizations about racial/ethnic disparities in overall birth defects-specific IMR.

The Black-White disparity for IMR due to abdominal wall defects observed in this study was not unidirectional/uniform for the two defect subtypes. Whereas Black infants with gastroschisis were twice as likely to die as Whites, Black babies with omphalocele were twice as likely to

survive the infancy period as Whites with the same defect. This shows that the natural history of omphalocele and gastroschisis differs by race in terms of survivability. One possible explanation for this finding could be the association of multiple defects with mortality. It has been observed that there is a direct dose-response relationship between presence of additional malformations and early mortality (Cleves et al., 2003). The extra malformations among White infants with omphalocele, albeit statistically non-significant, could result in their faster demise and worse survival probability as compared to Black infants with omphalocele. The univariate analysis we conducted showed that Black infants with omphalocele were less likely than Whites to have additional anomalies (38% versus 41.7%). However, the difference was very modest (3.7%) and not statistically significant. In addition, we controlled for the presence of multiple lesions in deriving the adjusted relative risk estimates, so this argument can hardly explain our findings. The same line of reasoning

Table 3
Adjusted Risk of Infant Mortality for Omphalocele and Gastroschisis by Race/Ethnicity

	Omphalocele		Gastroschisis	
	Crude HR	*Adjusted HR (95% confidence interval)	Crude HR	*Adjusted HR (95% confidence interval)
White, NH**	1.00	1.00 (—)	1.00	1.00 (—)
Hispanic	0.89	1.01 (0.68–1.48)	1.53	1.46 (0.77–2.77)
Black, NH**	0.52	0.52 (0.37–0.74)	2.31	2.23 (1.16–4.28)

*HR = hazard ratio. Adjusted estimates were generated by controlling for the confounding effects of maternal age, parity, maternal education, multiple anomalies, mode of delivery and level of care.

**NH = Non-Hispanic.

could be advanced for the Black-White disparity in favor of White infants with gastroschisis.

It has been postulated that omphalocele could be a relative of neural tube defect (NTD), being part of the same developmental field, namely, defect of the embryonic midline structures (Opitz, 1986), leading to the speculation that both could share similar pathogenetic pathways (Calzolari et al., 1997). In support of this hypothesis is the finding that periconceptional multivitamins containing folic acid could reduce the risk of non-syndromic omphalocele by 60% (Botto et al., 2002). This demonstrates that folic acid deficiency could be involved in the pathogenesis of omphalocele, just as it has been implicated in the genesis of NTD (Smithells et al., 1983; Berry et al., 1999; Czeizel and Dudas, 1992; MRC, 1991). Given this common pathway, it is reasonable to speculate that the natural history of the two defects (NTD and omphalocele) will be similar in terms of survival patterns during infancy. Although other investigators did report contradictory findings (Wong et al., 2001), Black infants with NTD have been shown to have better survival rates as compared to Whites with NTD (Davidoff et al., 2002), with the latter having an infant mortality rate that is 27% higher than that of the former. This enhanced survival of Black infants with NTD is analogous to our finding of lower mortality rates among Blacks with omphalocele, an interesting observation that raises the possibility that perhaps the two defects might be related not only in terms of etiologic pathways, but also in their natural history regarding survival patterns.

In a previous report (Salihu et al., 2003), we mentioned the likelihood of undercounts as a possible explanation for the drop in reported cases for the year 1998, and to a much lesser extent for 1999. We re-visited our data to determine whether under-reporting for those two years was racially or ethnically selective which could have impacted our results. We found that for each of the three racial/ethnic groups considered in this study, the level of reported cases (proportional distribution of cases by race) in 1998 and 1999 was within the expected range using previous years as referents. In addition, the two years comprised only about 8% of the reported cases over the 17-year period. Hence, it is unlikely that differential under-reporting based on race/ethnicity explained our findings.

It will be interesting to assess whether the racial differences in survival noted in this study are variably expressed among isolated and multiply malformed babies with abdominal wall defects. Such a study could enhance our current understanding regarding racial differences in survival among infants with these conditions. We are currently undertaking that study.

In summary, this study has demonstrated the existence of racial disparity in infant survival among babies born with abdominal wall defects. The better survival of Black infants with omphalocele and the higher mortality rates for Black infants with gastroschisis as compared to Whites is additional confirmation that the two malformations are different in origin, as well as natural history, with respect to survival. Our findings have implications for programs that are involved in setting and executing strategies to reduce racial/ethnic disparities in survival, especially among groups with developmental defects.

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LITERATURE CITED

- Anderson RN. 2001. Deaths: leading causes for 1999. *National Vital Statistics Reports*;49(11).
- Berger KH, Zhu B-P, Copeland G. 2003. Mortality throughout early childhood for Michigan children born with congenital anomalies, 1992-1998. *Birth Defects Research (Part A)* 67:656-661.
- Berry RJ, Li Z, Erickson JD, Li S, Moore CA, Wang H, Mulinare J, Zhao P, Wong LY, Gindler J, Hong SX, Correa A. 1999. Prevention of neural-tube defects with folic acid in China. China-US Collaborative Project for Neural Tube Defect Prevention. *N Engl J Med* 341:1485-1490.
- Botto LD, Mulinare J, Erickson DJ. 2002. Occurrence of omphalocele in relation to maternal multivitamin use: A population-based study. *Pediatrics* 109:904-908.
- Calzolari E, Bianchi F, Dolk H, Stone D, Milan M, and EUROCAT Working Group. 1997. Are Omphalocele and neural tube defects related congenital anomalies?: Data from 21 registries in Europe (EUROCAT). *Am J Med Genet* 72:79-84.
- Calzolari E, Bianchi F, Dolk H, Milan M, and EUROCAT Working Group. 1995. Omphalocele and gastroschisis in Europe: A survey of 3 million births 1980-1990. *Am J Med Genet* 72:79-84.
- Carpenter MW, Curci MR, Dibbins AW, Haddow JE. 1984. Perinatal management of ventral wall defects. *Obstet Gynecol* 64:646-651.
- Cleves MA, Gharrar S, Zhao W, Mosley BS, Hobbs CA. 2003. First-year survival of infants with congenital defects in Arkansas (1993-1998): A survival analysis using registry data. *Birth Defects Research (Part A)* 67:662-668.
- Czeizel AE, Dudas I. 1992. Prevention of the first occurrence of neural-tube defects by periconceptional vitamin supplementation. *N Engl J Med* 327:1832-1835.
- Davidoff MJ, Petrini J, Damus K, Russell RB, Mattison D. 2002. Neural tube defect-specific infant mortality in the United States. *Teratology* 66:S17-S22.
- Druschel C, Sharpe-S M, Cross P. Process of and problems in changing a birth defects registry reporting system. 2001. *Teratology* 64:S30-S36.
- Druschel CM, Hughes JP, Olsen C. 1996. Mortality among infants with congenital malformations, New York State, 1983-1988. *Public Health Rep* 111:359-365.
- Forrester MB, Merz RD. 1999. Epidemiology of abdominal wall defects, Hawaii, 1986-1997. *Teratology* 60:117-123.
- Honein M, Paulozzi L. 1999. Birth defects surveillance assessing the "gold standard". *Am J Public Health* 89:1238-1240.
- Lafferty PM, Emmerson AJ, Fleming PJ, Frank JD, Noblett HR. 1989. Anterior abdominal wall defects. *Arch Dis Child* 64:1029-1031.
- Martinez-Frias ML, Salvador J, Prieto L, Zaplana J. 1984. Epidemiological study of gastroschisis and omphalocele in Spain. *Teratology* 29:337-382.
- Morrow RJ, Whittle MJ, McNay MB, Raine PAM, Gibson AAM, Crossly J. 1993. Prenatal diagnosis and management of anterior abdominal wall defects in the West of Scotland. *Prenat Diagn* 13:111-115.
- MRC Vitamin Study Research Group. 1991. Prevention of neural tube defects: results of the Medical Research Council Vitamin Study. *Lancet* 338:131-137.
- Opitz JM, ed(1986): "The Developmental Field Concept." New York: Alan Liss, Inc.
- Petrini J, Damus K, Russell R, Poschman K, Davidoff MJ, Mattison D. 2002. Contribution of birth defects to infant mortality in the United States. *Teratology* 66:S3-S6.
- Rankin J, Dillon E, Wright C. 1999. Congenital Anterior Wall Defects in the North of England, 1986-1996: Occurrence and Outcome. *Prenat Diagn* 19:662-668.
- Salihu HM, Boos R, Schmidt W. Omphalocele and gastroschisis. 2002. *J Obstet Gynaecol* 22:489-492.
- Salihu HM, Pierre-Louis BJ, Druschel CM, Kirby RS. 2003. Omphalocele and gastroschisis in the state of New York, 1992-1999. *Birth Defects Research (Part A)* 67:630-636.
- Smithells RW, Nevin NC, Seller MJ, Sheppard S, Harris R, Read AP, Fielding DW, Walker S, Schorah CJ, Wild J. 1983. Further experience of vitamin supplementation for prevention of neural tube defect recurrences. *Lancet* 1:1027-1031.
- Tan KH, Kilby MD, Whittle MJ, Beatie BR, Booth IW, Botting BJ. 1996. Congenital anterior abdominal wall defects in England and Wales 1987-93: retrospective analysis of OPCS data. *Br Med J* 313:903-906.
- Torfs C, Curry C, Roeper P. 1990. Gastroschisis. *J Pediatr* 116:1-6.
- Wong L-Y C, Paulozzi LJ. 2001. Survival of infants with spina bifida: a population study, 1979-94. *Paediatr Perinat Epidemiol* 15:374-378