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Maternal race, demography and health care disparities impact risk for IVH in preterm neonates

Seetha Shankaran, MD¹, Aiping Lin, MD², Jill Maller-Kesselman, MS², Heping Zhang, PhD³, T. Michael O'Shea, MD⁴, Henrietta S. Bada, MD⁵, Jeffrey R. Kaiser, MD MA⁶, Richard P. Lifton, MD, PhD⁷, Charles R. Bauer, MD^{8,*}, and Laura R. Ment, MD^{2,9,*} on behalf of the Gene Targets for Intraventricular Hemorrhage^{**}

¹Department of Pediatrics, Wayne State University School of Medicine, Detroit, MI

²Department of Pediatrics, Yale University School of Medicine, New Haven, CT

³Department of Epidemiology and Public Health, Yale University School of Medicine, New Haven, CT

⁴Department of Pediatrics, Wake Forest School of Medicine, Winston Salem, NC

⁵Department of Pediatrics, University of Kentucky College of Medicine

⁶Departments of Pediatrics and Obstetrics and Gynecology, Baylor College of Medicine, Houston, TX

⁷Department of Genetics and the Howard Hughes Medical Institute, Yale University School of Medicine, New Haven, CT

⁸Department of Pediatrics, University of Miami Miller School of Medicine

⁹Department of Neurology, Yale University School of Medicine, New Haven, CT

Abstract

Objective—To determine whether risk factors associated with Grade (Gr) 2–4 intraventricular hemorrhage (IVH) differs between African ancestry and white subjects.

Study design—Inborn, appropriate for gestational age (GA) infants with birth weights (BW) 500–1250 grams and exposed to >1 dose of antenatal steroids were enrolled in 24 neonatal intensive care units. Cases had Gr 2–4 IVH and controls matched for site, race and BW range had 2 normal ultrasounds read centrally. Multivariate logistic regression modeling identified factors associated with IVH across African ancestry and white race.

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Corresponding author: Seetha Shankaran MD, Children's Hospital of Michigan, 3901 Beaubien Blvd., Detroit, MI 48201, Phone: 313-745-1436 Fax: 313-745-5568, sshankar@med.wayne.edu.

*Contributed equally

**A list of members of the Gene Targets for IVH Study is available at www.jpeds.com (Appendix).

The authors declare no conflicts of interest.

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Results—Subjects included 579 African ancestry or white race infants with Gr 2–4 IVH and 532 controls. Mothers of African ancestry children were less educated, and white case mothers were more likely to have > 1 prenatal visit and have a multiple gestation ($P = .01$ for all). Increasing GA ($P = .01$), preeclampsia ($P < .001$), complete antenatal steroid exposure ($P = .02$), cesarean delivery ($P < .001$) and white race ($P = .01$) were associated with decreased risk for IVH. Chorioamnionitis ($P = .01$), Apgar < 3 at 5 min ($P < .004$), surfactant ($P < .001$) and high frequency ventilation ($P < .001$) were associated with increased risk for IVH. Among African ancestry infants, having >1 prenatal visit was associated with decreased risk ($P = .02$). Among white infants, multiple gestation was associated with increased risk ($P < .001$) and higher maternal education with decreased IVH risk ($P < .05$).

Conclusion—Risk for IVH differs between African ancestry and white infants and may be attributable to both race and health care disparities.

Keywords

preterm infant; intraventricular hemorrhage; race; multiple gestation; prenatal care

Intraventricular hemorrhage (IVH) is a developmental disorder with significant neurodevelopmental morbidity.[1–7] Often attributed to alterations in cerebral blood flow to the immature germinal matrix microvasculature, IVH occurs against the backdrop of preterm birth in which risk and protective environmental factors have long been known.[8–12]

Women of African ancestry are at greater risk for preterm labor and delivery than white women,[13–16] and, even in the era of sophisticated perinatal intensive care strategies, a disproportionate number of very low birth weight infants are born to African ancestry mothers.[14, 15] Compared with white women, more African ancestry women who deliver prematurely have inadequate prenatal care and less education, and their neonates are less likely to receive surfactant or assisted ventilation.[17] There is a 2-fold higher rate of IVH-related mortality in African ancestry neonates,[18] suggesting that both preterm birth and its sequelae reflect the interaction of race and health care disparities.

Lower gestational age (GA) and birth weight (BW), male sex, white race, neonatal transport, chorioamnionitis, illness severity, delivery room resuscitation, assisted ventilation, and respiratory distress syndrome and its complications are associated with increased risk for IVH, and antenatal corticosteroids, cesarean delivery and preeclampsia are all correlated with a decreased risk for hemorrhage.[19–24] However, advances in neonatal and perinatal care and the increased survival of extremely low birth weight infants may have altered these associations.[25] The contribution of race and healthcare disparity to the incidence of IVH remains largely unexplored. The objective of this report is to evaluate whether risk factors associated with IVH differ in a recent, prospective cohort of appropriate for GA for African ancestry and white inborn infants exposed to partial or complete course of antenatal steroid exposure and whose cranial ultrasounds were centrally read [26, 27].

METHODS

Infants born June 1, 2007, and October 31, 2012, with BW 500–1250g with Grade (Gr) 2–4 IVH and matched infants with normal cranial ultrasound of the same BW range were enrolled into a prospective study of the environmental and genetic risk factors for IVH at 24 university-affiliated hospitals in the US and Sweden. The study procedures and protocols were reviewed and approved by the institutional review boards of each participating institution. Written informed consent was obtained from the parent(s)/guardian(s) from cases and controls.

Case infants were eligible if they had Gr 2–4 IVH based upon masked review of cranial ultrasound by sonographers and met the following criteria: (1) inborn; (2) exposed to at least one dose of antenatal steroid exposure; (3) BW 500–1250 g; (4) appropriate size for GA; [28] (5) no evidence of congenital or chromosomal disorders or infections; (6) no family history of coagulopathy; and (7) not a sibling of an enrolled subject. Control infants met these criteria, had two normal cranial ultrasound within the required time intervals described below and were matched to cases based on the following criteria: (1) site; (2) sex; and (3) BW range (ie, 500–749 g; 750–999 g; 1000–1250 g). In addition, every effort was made to match controls based on self-reported maternal race and ethnicity. Enrollment was limited to one sibling of a multiple birth set; if more than one sibling of a multiple birth set had IVH, then the sibling to be included as a case was randomly selected. If both multiples had the same grade of IVH, the one enrolled was selected from a random table; if not similar, the one with the higher grade of IVH was enrolled.

Eligibility and study group were based upon clinical cranial ultrasound. Cases had Gr 2–4 IVH within the first 28 postnatal days (PND); controls had 2 normal cranial ultrasound, the first within day 5–10 and the second within PND 21–35, both without IVH, germinal matrix hemorrhage (GMH), periventricular leukomalacia, ventriculomegaly or central nervous system malformations. The grading system for Gr 2–4 IVH follows Papile et al: [29] Gr 2, GMH with blood within the ventricular system; Gr 3, GMH with blood filling at least 50% of the ventricular system and ventricles measuring at least 1.1 cm at the mid-body of the lateral ventricle on a sagittal scan; Gr 4, GMH with intraventricular and intraparenchymal hemorrhage. Although initial screening was based on imaging reports from patient records, eligibility was confirmed by at least one site sonographer who had successfully completed standardized online study training showing images of GMH, grades 2 - 4 IVH and ventriculomegaly. All site sonographers were required to pass an online quiz composed of 10 different sets of ultrasound images prior to being “certified” to read the site ultrasounds for study enrollment.

Following subject enrollment, cranial ultrasound were submitted for central review by at least one of four study sonographers masked to the subjects’ case-control status. Eligibility and group assignment were based upon the following criteria: GMH, ventriculomegaly and Gr IVH. Images were sent to a second masked sonographer for review when the site and central readings were not in agreement. When both central reviewers concurred that images did not support eligibility, the subject was excluded. If the two disagreed, images were sent to the study’s head sonographer for final review.

Data were collected from medical records and entered into a secure online database housed at Yale University. Maternal data included age, highest level of education, prenatal care, primary medical insurance, maternal magnesium sulfate < 72 hours prior to delivery, preeclampsia, clinical chorioamnionitis and antenatal steroid exposure < 7 days prior to birth.

Delivery room variables included Apgar scores and need for resuscitation. Neonatal data included early receipt of indomethacin within first 6–12 hours following birth, caffeine within first 2 PND, high frequency ventilation (HFV) within the first 7 PND, GA, BW, sex, multiple birth, and reported race and ethnicity. In addition, data for surfactant, pneumothorax and seizures were collected for the first 28 PND. Data definitions are provided in Table I (available at www.jpeds.com).

The neonates in this report are part of an ongoing study investigating the genetic and environmental contributions to IVH, and 1100 of the 1111 (99%) infants had a genetic assessment of race.[30, 31]

Statistical Analyses

The primary outcome was Gr 2–4 IVH. Continuous variables were analyzed using Student t-test or Wilcoxon Rank-Sum test and categorical variables were analyzed using Fisher exact test, comparing African ancestry cases vs. African ancestry controls, white cases vs. white controls, all cases vs. all controls, and African ancestry cases vs. white cases. Stratified categorical data were analyzed using the Mantel Haenzel test. To identify risk factors independently and significantly associated with Gr 2–4 IVH a multivariate logistic regression model was built based on the stepwise variable selection using site, significant variables in the univariate analyses (all cases vs. all controls) and their interactions with race. Post-hoc univariate analyses were performed with selected data for African ancestry vs. white cases and for those variables with significant raceinteraction terms in the logistic regression model. For all analyses, SAS (version 9.3) was used and $P < .05$ was considered statistically significant.

RESULTS

During the study period, 12, 022 infants were screened for study eligibility at the participating sites (Figure; available at www.jpeds.com). There were 981 infants with Gr 2–4 IVH who met eligibility criteria as cases; of these 146 infants died in the NICU. Infants who died prior to enrollment had lower birth weight than infants enrolled in the study (data not shown). Consent was obtained for 626 case infants; 579 were African ancestry or white race and were enrolled. Case infants excluded were: 18 Asian, 15 > one race, 2 American Indian/Alaska Native, 2 Native Hawaiian/other Pacific Islander, and 10 unknown. 532 control infants were enrolled; these 1,111 infants (579 cases and 532 controls) form the basis of this report.

Significantly lower BWs and GA were noted among all cases compared with all control infants and within the African ancestry cases vs. control and white cases vs. control groups (Table II). Although cases were more likely to have been products of multiple gestation

pregnancies, this association was significantly more common among white rather than African ancestry infants.

Among the maternal characteristics (Table III), case mothers had a higher rate of clinical chorioamnionitis, but a lower frequency of preeclampsia, compared with all control mothers, and within the African ancestry cases vs. control and white cases vs. control groups. In the whole cohort and among African ancestry infants, case mothers were also less likely to have at least one prenatal visit or to have received magnesium sulfate or a complete course of antenatal steroid exposure than mothers of controls (Table IV). White case infants were also less likely to have received antenatal steroid exposure than controls. African ancestry case mothers had lower levels of education; 23.0% reporting < high school education compared with 16.0% white case mothers ($P < .001$ for highest level of education). Medicaid was the primary insurance for 67.4% of African ancestry case mothers compared with 39.2% of white case mothers ($P < .001$ across all insurance). At least one prenatal visit was documented among 92.1% African ancestry case mothers compared with 97.3% mothers of white cases ($P = .006$). Similarly, African ancestry mothers were less likely to have received a complete course of antenatal steroid exposure (41.3 vs. 50.7%, $P = .03$).

Neonatal characteristics are shown in Table V. Cases (overall and among African ancestry and white infants) were less likely than controls to have been delivered by cesarean delivery, had a higher rate of Apgar scores < 3 at both 1 and 5 min and were more likely to require intubation for resuscitation, chest compressions and epinephrine in the delivery room. Cases were less likely to have received CPAP for resuscitation but more likely to have been treated with HFV during the first postnatal week and to have received surfactant. Cases more often experienced both pneumothoraces and seizures when compared with controls.

Comparison of African ancestry and white cases revealed that African ancestry infants were more likely to have one min ($P = .002$) but not five min Apgar scores < 3. African ancestry cases were also more likely than white cases to receive epinephrine ($P = .01$) but less likely to receive surfactant ($P = .005$).

Demographics, Health Care, and the Risk for IVH

The model shown in Table VI (OR, 95%CI) demonstrates that increasing GA, preeclampsia, a complete course of antenatal steroid exposure, cesarean delivery and white race were associated with decreased risk for IVH. In contrast, chorioamnionitis, Apgar < 3 at 5 min, surfactant and HFV increased risk for IVH. Multiple gestation increased risk for IVH only for white infants. Having at least 1 prenatal visit decreased risk for African ancestry neonates and maternal college education was associated with a lower risk for IVH for white infants.

Exploratory Post Hoc Analyses

To further explore the variable-by-racial interaction terms that were independent and important predictors of Gr 2–4 IVH in the model, exploratory *post hoc* analyses were performed. Overall white mothers were more likely to have had *in vitro* fertilization (IVF) for pregnancy induction compared with African ancestry mothers [31/659 (4.7%) compared

with 4/452 (0.9%), $P < .001$). In addition, white mothers with multiple gestation pregnancies tended to have more IVF induced pregnancies [white vs. African ancestry: 22/181 (12.2%) vs. 2/67 (3.0%), $P = .03$]. Because of a potential white-IVF bias, the race-by-multiple gestation analysis was repeated while excluding IVF assisted pregnancies and the results were unchanged ($P < .001$).

DISCUSSION

After controlling for confounding variables in this well-characterized case-control study, relative to white preterm infants, African ancestry neonates were observed to be at significantly increased risk of Gr 2–4 IVH. This is the first study to report that for developing Gr 2–4 IVH, the previously demonstrated protective effect of being African ancestry as a preterm infant [32] is no longer evident. African ancestry mothers had more evidence of risk, including inadequate prenatal care and lower maternal educational and insurance status; similarly, their infants had less antenatal steroid exposure and, most likely secondarily, a greater need for resuscitation. The potential causes of our reported new observation are likely multifactorial and may relate both to access to care and to uneven distribution of medical resources. Absence of prenatal care has previously been shown to increase risk of IVH, but the influence of race on this finding has not been previously explored.[33, 34] In our study, if the mothers had at least one prenatal visit, the risk for IVH among African ancestry infants significantly declined, suggesting that initiating maternal/fetal care prior to labor and delivery provides a distinct protective advantage.

We also report for the first time that multiple gestation pregnancies were associated with a higher risk of Gr 2–4 IVH for white neonates only. The published associations of plurality and 12 IVH report mixed results, but none include race in their analyses.[35–38] In our study, mothers of white IVH cases were more likely to be older, undergo IVF and experience cesarean delivery compared with African ancestry case mothers; these factors alone may not explain this association. Previous studies have not confirmed an association between IVF, multiple gestation and IVH; race was not included in these analyses.[23, 35, 39, 40] Our observation will need to be explored in additional cohorts.

We did examine the birth weight, gestational age and educational status of the cohort enrolled in Sweden compared with that in this country; the average birth weight and gestational age was lower and the educational status higher in the Swedish cohort (data not shown). The model for risk of IVH was analyzed with and without the inclusion of subjects from Sweden, the model for risk remained unchanged.

In our study, white infants whose mother had at least a college education had a decreased risk for IVH compared with African ancestry infants of mothers with college educations. It has been demonstrated that compared with white women, a higher percentage of African ancestry women who deliver prematurely have less post-high school education,[14–16, 41] but the association of education and IVH has been previously unexplored.

Finally, our study includes neonates from both the United States and Sweden, countries with different health care systems. The Swedish neonates had lower birth weights and gestational

ages and higher levels of maternal education than infants born in the US. Notably, the model for IVH was unchanged when these subjects were excluded, confirming the validity of our findings.

The strengths of this study include the large and well-characterized cohort of appropriate for GA inborn neonates with at least exposure to a partial course of antenatal steroid exposure, centrally read cranial ultrasound and genotypes characterizing race. IVH is lower in infants exposed to a partial course compared with no antenatal steroid exposure, and lower with exposure to complete compared with partial antenatal steroid exposure (32); hence our cohort serves to interrogate emerging demographic and environmental risk for IVH.

A study limitation is lack of data regarding the number and timing of prenatal health visits. In addition, we do not have either the time of onset for IVH nor measures of thrombophilia, as atypical timing of IVH may be characterized by evidence of coagulopathy.[42] We did not collect physiologic measures of the cerebral circulation.[43, 44] Injury to the white matter of the brain is an important cause of neurodevelopmental impairment; we did not evaluate magnetic resonance imaging studies to detect white matter injury. Finally, the incidence of multiple gestation pregnancies in white mothers was almost double that in African ancestry mothers in our study and that finding may have influenced the analysis. However, preterm multiple births have been reported to be more frequent in the white population than in African ancestry women [45, 46] and may be attributable to differences in the use of assisted reproduction technology.[47–49] The analysis of our data omitting all neonates from IVF-induced pregnancies confirmed our primary findings.

Preterm birth represents one of the major pediatric public health problems of our time, and IVH is a significant morbidity of the prematurely born. Although we show that risk for Gr 2–4 IVH is greater among African ancestry compared with white infants, this finding is reduced by maternal attendance at a single prenatal visit. In addition, multiple gestation pregnancies were associated with a higher risk of Gr 2–4 for white infants only, suggesting underlying epigenetic or additional genetic factors. The high social and medical risk status of the mothers in this study reflects both racial and healthcare disparities between our groups and stresses the critical public health implications for the prevention of IVH in the prematurely-born.

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ABBREVIATIONS

BW	Birth weight
GA	Gestational age
GMH	Germinal matrix hemorrhage

Gr	Grade
HFV	High frequency ventilation
IVH	Intraventricular hemorrhage
IVF	In-vitro fertilization
PND	Postnatal day

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Appendix

Members of the Gene Targets for IVH Study include:

Baylor College of Medicine, Texas Children's Hospital and Ben Taub General Hospital: Cindy Bryant, BSN, CCRN, CCRP, Christopher Cassady, MD, Carmen Garcia, RN, BSN, Yvette R. Johnson, MD, MPH, Heidi E. Karpen, MD, Diane Kent, RN, Martha M. Munden, MD, Geneva Shores, RNC-LRN; Brown University and Women & Infants Hospital: John

Cassese, MD, Angelita M. Hensman, RN, BSN, Elisa Vieira, BS, RN, Betty Vohr, MD, Michael Wallach, MD; East Carolina University, Brody School of Medicine: James J. Cummings, MD, Scott S. MacGilvray, MD, Sherry Moseley, RN, Vickie Trapanotto, MD; Foundation for Blood Research: Walter Allan, MD; Indiana University School of Medicine and Riley Hospital for Children: Leslie R. Delaney, MD, Faithe Hamer, Brenda Poindexter, MD, Leslie Dawn Wilson, BS, CCRC, Shirley Wright-Coltart, RN, CCRP; Karolinska Institutet, Karolinska University Hospital: Ulrika Ådén, MD, PhD, Marco Bartocci, MD, PhD, Hugo Lagercrantz, MD, Gordana Printz, RN, BSc; Loma Linda University School of Medicine: Lila Dalton, RN, CCRP, Andrew Hopper, MD, Leon Smith, LVN, CCRP, Kimberly Victor, PhD, RN, Betty Voltz, LVN, CRC, Beverly P. Wood, MD, Lionel Young; Sahlgrenska Academy at the University of Gothenburg, Queen Silvia Children's Hospital: Jessica Alfsson, RN, Karin Sävman, MD, PhD; University of Alabama at Birmingham, Women's and Infants' Center: Waldemar Carlo, MD, Monica Collins, RN, MAED, Stuart A. Royal, MS, MD, Daniel W. Young, MD, Shirley Cosby, RN, BSN, Crystal Helms, RN, BSN; University of Arkansas for Medical Sciences: Teresita Angtuaco, MD, Jeffrey R. Kaiser, MD MA, N. Carol Sikes, BSN, MScN, Melanie J. Mason, RN, R. Whit Hall, MD; University of Kentucky: Henrietta Bada, MD, MPH, Harigovinda R. Challa, MD, Deborah L. Grider, RN, Vesna Kriss, MD, Tracey Robinson, RN, Vicki Whitehead, RN, CCRC; University of Miami–Leonard M. Miller School of Medicine, Holtz Children's Hospital: George Abdenour, MD, Charles Bauer, MD, Gary Danton, MD, Daniel Montesinos, BA, Saigal Gaurav, MD, Willy Philiass, MD, Uygur Teomete, MD; University of Michigan: John Barks, MD, PhD, Mary Christensen, BA, RRT, Ramon Sanchez, MD, Makayla Sieg, BSHA, Stephanie Wiggins, BS; University of New Mexico Health Science Center: Janell Fuller, MD, Lucille Papile, MD, Carol Hartenberger, RN, MPH, Connie Backstrom Lacy, RN, CCRC, Rebecca Montman, BSN, RNC, Julie Rohr, MSN, RNC, Jessica B. Williams, MD, Susan Williamson, MD; University of North Carolina at Chapel Hill, University of North Carolina Children's Hospital: Carl Bose, MD, Cynthia L. Clark, RN, Matthew Laughon, MD, MPH; University of Pennsylvania, Pennsylvania Hospital: Soraya Abbasi, MD, Noah M. Cook MD, MTR, Toni Mancini RN, CCRC, BSN; University of Pennsylvania, Children's Hospital of Philadelphia, Hospital of the University of Pennsylvania: African ancestries Chaudhary BS, RRT, Christopher DeMauro, MD, Barbara Schmidt, MD, MSc; University of South Alabama, Children's and Women's Hospital: Ellen Dean, RNC, BS, Fabien Eyal, MD, Paul Maertens; University of Tennessee Health Sciences Center, the Regional Medical Center Hospital: Thomas F. Boulden, MD, Harris L. Cohen, MD, Shelia Dempsey, RN, CCRC, Pam LeNoue, RN, Massroor Pourcyrus, MD; University of Utah and Intermountain Healthcare: Karie Bird, RN, BSN, Jill J. Burnett, BSN, Laura Cole, RN, Roger G. Faix, MD, Gary Hedlund, OD, Kevin Moore, MD, Manndi Loertscher, Karen Osborne, RN, BSN, CCRC, Carrie Rau, RN; Cindy Spencer, BSN, Kimberlee Weaver-Lewis MS, RN, Bradley A. Yoder, MD; University of Washington: Amanda T. Jones, BA, Dennis E. Mayock, MD, Manjiri Dighe, MD; Wake Forest School of Medicine, Forsyth Medical Center, Brenner Children's Hospital: Patricia L. Brown, RN, T. Michael O'Shea, MD, Nancy Peters, RN; Washington University in St. Louis, the St. Louis Children's Hospital: Terrie Inder, MBChB, MD, Karen Lukas, RN, Amit Mathur, MD, Robert McKinstry, MD, Joshua Shimony, MD, Jennifer Walker; Wayne State University, Children's Hospital of Michigan, Hutzel Women's Hospital: Aparna Joshi,

MD, Jay Ann Nelson, BSN, Seetha Shankaran, MD, Eunice H. Woldt, MSN; Yale University School of Medicine: Kenneth Baker, MD, Matthew J. Bizzarro, MD, Charles Duncan, MD, Richard Ehrenkranz, MD, Anita Farhi, RN, T.R. Goodman, MBChB, MD, Murat Gunel, MD, Jeffrey R. Gruen, MD, Karol Katz, MS, Monica Konstantino RN, BSN, Zhifa Liu, MS, Erin Loring, MS, CGC, Robert W. Makuch, PhD, Carol Nelson-Williams, PhD, JoAnn Poulsen, RN, Karen Schneider, MPH, Jan Taft, RN. Additional collaborators include:

ELGAN Study: Elizabeth Newton Allred, MS (Department of Biostatistics, Harvard School of Public Health; Department of Neurology, Children's Hospital Boston), Alan Leviton, MD, (Department of Neurology, Children's Hospital Harvard); Oulu University: Mikko Hallman, MD, PhD (Department of Pediatrics, University of Oulu), Johanna Huusko, MSc (Department of Pediatrics); University of Iowa: Susan K. Berends, MA (Department of Pediatrics), Allison M. Momany, BS (Department of Pediatrics), Jeffrey C. Murray, MD, (Department of Pediatrics, University of Iowa College of Medicine; Department of Biological Sciences, University of Iowa College of Liberal Arts; Department of Preventive Medicine and Department of Epidemiology, University of Iowa), Nancy J. Weathers (College of Nursing).

Figure 1.
Details of the study population

Data Definitions

Table 1

Variable	Definition
Clinical chorioamnionitis	Two or more of the following criteria in the absence of other diseases: fetal tachycardia, maternal tachycardia, uterine tenderness or maternal fever of >100.4 degrees F. Histologic evidence of chorioamnionitis without the presence of other symptoms was not coded as chorioamnionitis
Complete course of antenatal steroids	Complete course of betamethasone: 2 doses given 12–24 hours apart; complete course of dexamethasone: 4 doses given 6–12 hours apart.
High frequency ventilation	High frequency oscillatory or jet ventilation in the first 7 postnatal days.
Intubation for resuscitation in delivery room	Infant was intubated in the delivery room for resuscitation, or if intubated for surfactant administration, remained intubated until stabilized in the NICU.
Multiple gestation	Gestation resulting in > 1 live birth, in which more than one embryo was successfully implanted, including those in which fetal demise or reduction occurred.
Preeclampsia	Sustained elevation in blood pressure of >140 systolic and/or >90 diastolic, accompanied by proteinuria, after 20 weeks gestation in a previously normotensive woman.
Prenatal care	At least one visit during the pregnancy leading to the subject's birth.
Prophylactic indomethacin	Indomethacin administered for the prevention of IVH within 6–12 postnatal hours.

Table II

Demographics of Study Subjects

	African Ancestry			White			African Ancestry and White		
	IVH Gr 2-4 Cases	Controls	P Value	IVH Gr 2-4 Cases	Controls	P Value	IVH Gr 2-4 Cases	Controls	P Value
Number of subjects	242	210		337	322		579	532	
Birth weight (N,SD)	776 (242, 185)	818 (210, 183)	0.016	814 (337, 184)	851 (322, 173)	0.009	798 (185)	838 (178)	0.003
GA wks (N,SD)	25.5 (242, 1.7)	26.3 (210, 1.8)	<.001	25.6 (337, 1.6)	26.6 (322, 1.6)	<.001	25.6 (1.6)	26.4 (1.7)	<.001
Male subjects (%)	141/242 (58.3)	113/210 (53.8)	0.34	196/337 (58.2)	176/322 (54.7)	0.39	337/579 (58.2)	289/532 (54.3)	0.20
Hispanic (%)	3/242 (1.2)	4/210 (1.9)	0.71	54/337 (16.0)	48/322 (14.9)	0.75	57/579 (9.8)	52/532 (9.8)	1
Grade 2 (%)	90 (37.2)			109 (32.3)			199 (34.4)		
Grade 3 (%)	53 (21.9)			96 (28.5)			149 (25.7)		
Grade 4 (%)	99 (40.9)			132 (39.2)			231 (39.9)		
Multiple gestation (%)	37/242 (15.3)	30/210 (14.3)	0.79	113/337 (33.5)	68/322 (21.1)	<.001	150/579 (25.9)	98/532 (18.4)	0.003

Abbreviation: (SD), Standard Deviation; N/A, not applicable

Table III

Maternal Characteristics

	African Ancestry			White			African Ancestry and White		
	IVH Gr 2-4 Cases	Controls	P Value	IVH Gr 2-4 Cases	Controls	P Value	IVH Gr 2-4 Cases	Controls	P Value
Maternal Age (N, SD)	25.8(240, 6.3)	26.8(204, 6.3)	0.11	27.7 (316, 6.5)	28.1 (300, 6.6)	0.45	26.9 (556, 6.5)	27.6 (504, 6.5)	0.09
Highest Level of Maternal Education									
Less than High School (%)	55/239 (23.0)	34/205 (16.6)	0.33	53/332 (16.0)	50/317 (15.8)	0.29	108/571 (18.9)	84/522 (16.1)	0.33
HS Grad or GED (%)	87/239 (36.4)	85/205 (41.5)		101/332 (30.4)	76/317 (24.0)		188/571 (32.9)	161/522 (30.8)	
Some college (%)	76/239 (31.8)	64/205 (31.2)		86/332 (25.9)	91/317 (28.7)		162/571 (28.4)	155/522 (29.7)	
4 year college degree (%)	21/239 (8.8)	22/205 (10.7)		92/332 (27.7)	100/317 (31.5)		113/571 (19.8)	122/522 (23.4)	
Gravida ^a (N, range)	2 (242, 1-11)	3 (210, 1-15)	0.15	2 (337, 1-14)	2 (322, 1-15)	0.16	2 (579, 1-14)	2 (532, 1-15)	0.78
Parity ^a (N, range)	2 (242, 1-9)	2 (210, 1-9)	0.15	2 (337, 1-8)	1 (322, 1-7)	0.04	2 (579, 1-9)	2 (532, 1-9)	0.55
Clinical chorioamnionitis (%)	95/242 (39.3)	50/210 (23.8)	<.001	109/337 (32.3)	65/322 (20.2)	<.001	204/579 (35.2)	115/532 (21.6)	<.001
Preeclampsia (%)	23/242 (9.5)	71/210 (33.8)	<.001	34/336 (10.1)	85/321 (26.5)	<.001	57/578 (9.9)	156/531 (29.4)	<.001

^aMedian value

Prenatal Care

^a Administered within 72 hours prior to delivery

Table V

Neonatal Characteristics

	African Ancestry			White			African Ancestry and White		
	IVH Gr 2-4 Cases	Controls	P Value	IVH Gr 2-4 Cases	Controls	P Value	IVH Gr 2-4 Cases	Controls	P Value
Delivery Room Variables									
Apgar score < 3									
At 1 minute (%)	117/242 (48.3)	70/210 (33.3)	0.002	119/337 (35.3)	80/322 (24.8)	0.004	236/579 (40.8)	150/532 (28.2)	<.001
At 5 minutes (%)	30/242 (12.4)	9/210 (4.3)	0.002	40/337 (11.9)	15/322 (4.7)	0.001	70/579 (12.1)	24/532 (4.5)	<.001
Delivery by cesarean (%)	129/242 (53.3)	145/210 (69.0)	<.001	193/337 (57.3)	238/322 (73.9)	<.001	322/579 (55.6)	383/532 (72.0)	<.001
Bag and mask ventilation (%)	210/241 (87.1)	169/210 (80.5)	0.07	297/337 (88.1)	274/322 (85.1)	0.25	507/578 (87.7)	443/532 (83.3)	0.04
CPAP (%)	57/242 (23.6)	70/210 (33.3)	0.03	79/337 (23.4)	120/322 (37.3)	<.001	136/579 (23.5)	190/532 (35.7)	<.001
Intubation for resuscitation (%)	208/242 (86.0)	139/210 (66.2)	<.001	277/337 (82.2)	207/322 (64.3)	<.001	485/579 (83.8)	346/532 (65.0)	<.001
Chest compressions (%)	29/242 (12.0)	14/210 (6.7)	0.08	36/337 (10.7)	19/322 (5.9)	0.03	65/579 (11.2)	33/532 (6.2)	0.004
Epinephrine (%)	25/242 (10.3)	7/210 (3.3)	0.005	16/337 (4.7)	10/322 (3.1)	0.32	41/579 (7.1)	17/532 (3.2)	0.004
Neonatal Interventions									
Prophylactic indomethacin ^a (%)	51/242 (21.1)	61/210 (29.0)	0.063	94/337 (27.9)	83/322 (25.8)	0.60	145/579 (25.0)	144/532 (27.1)	0.45
High frequency ventilation ^b (%)	225/242 (93.0)	164/210 (78.1)	<.001	324/337 (96.1)	266/322 (82.6)	<.001	549/579 (94.8)	430/532 (80.8)	<.001
Surfactant ^c (%)	107/242 (44.2)	42/209 (20.1)	<.001	189/337 (56.1)	73/322 (22.7)	<.001	296/579 (51.1)	115/531 (21.7)	<.001
Neonatal degree of illness and morbidities									
Pneumothorax ^c (%)	18/242 (7.4)	5/210 (2.4)	0.02	39/337 (11.6)	12/322 (3.7)	<.001	57/579 (9.8)	17/532 (3.2)	<.001
Multiple seizures ^c (%)	8/239 (3.3)	0/210 (0)	0.008	8/325 (2.5)	3/319 (0.9)	0.22	16/564 (2.8)	3/528 (0.6)	0.004

^a 6-12 postnatal hours;^b 1-7 postnatal days;^c 1-28 postnatal days

Table VI

Logistic regression model for risk for IVH with all African ancestry and white subjects

Effect	p-value	OR	95% Confidence Limits	
GA weeks	0.01	0.89	0.82	0.97
Clinical chorioamnionitis	0.01	1.48	1.08	2.02
Preeclampsia	0.001	0.52	0.35	0.76
Complete course antenatal steroids	0.02	0.71	0.54	0.94
Apgar score < 3 at 5	0.004	2.13	1.27	3.59
Cesarean delivery	<.0001	0.50	0.37	0.67
Surfactant	<.0001	3.32	2.06	5.34
High frequency ventilation	<.0001	2.61	1.94	3.51
White race	0.012	0.26	0.09	0.75
College degree x white	0.047	0.70	0.49	0.99
Prenatal visit x African ancestry	0.02	0.29	0.10	0.82
Multiple gestation x White	<.0001	2.28	1.51	3.45