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Retinal and Optic Nerve Hemorrhages in the Newborn Infant

One-Year Results of the Newborn Eye Screen Test Study

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Purpose: To report the birth prevalence, risk factors, characteristics, and location of fundus hemorrhages (FHs) of the retina and optic nerve present in newborns at birth.

Design: Prospective cohort study at Stanford University School of Medicine.

Participants: All infants who were 37 weeks postmenstrual age or older and stable were eligible for screening. Infants with known or suspected infectious conjunctivitis were excluded.

Methods: Infants born at Lucile Packard Children's Hospital (LPCH) from July 25, 2013, through July 25, 2014, were offered universal newborn screening via wide-angle digital retinal photography in the Newborn Eye Screen Test study. Maternal, obstetric, and neonatal factors were obtained from hospital records. The location, retinal layer, and laterality of FH were recorded by 1 pediatric vitreoretinal specialist.

Main Outcome Measures: Birth prevalence of FH. Secondary outcomes included rate of adverse events, risk factors for FH, hemorrhage characteristics, and adverse events.

Results: The birth prevalence of FH in this study was 20.3% (41/202 infants). Ninety-five percent of FHs involved the periphery, 83% involved the macula, and 71% involved multiple layers of the retina. The fovea was involved in 15% of FH cases (birth prevalence, 3.0%). No cases of bilateral foveal hemorrhage were found. Fundus hemorrhages were more common in the left eye than the right. Fundus hemorrhages were most commonly optic nerve flame hemorrhages (48%) and white-centered retinal hemorrhages (30%). Retinal hemorrhages were found most frequently in all 4 quadrants (35%) and more often were multiple than solitary. Macular hemorrhages most often were intraretinal (40%). Among the risk factors examined in this study, vaginal delivery compared with cesarean section (odds ratio [OR], 9.34; 95% confidence interval [CI], 2.57−33.97) showed the greatest level of association with FH. Self-identified ethnicity as Hispanic or Latino showed a protective effect (OR, 0.43; 95% CI, 0.20−0.94). Other study factors were not significant.

Conclusions: Fundus hemorrhages are common among newborns. They often involve multiple areas and layers of the retina. Vaginal delivery was associated with a significantly increased risk of FH, whereas self-identified Hispanic or Latino ethnicity was protective against FH in this study. The long-term consequences of FH on visual development remain unknown. *Ophthalmology 2016;■:1−10 © 2016 by the American Academy of Ophthalmology.*

Studies conducted outside of the United States on ethnically homogenous populations report the incidence of birth-related fundus hemorrhages (FHs) to be between 2.6% and 50%.[1−4] The mechanism of increased risk of FH during a vaginal delivery is hypothesized as follows: passage of the head through the canal can cause an acute rise in intracranial pressure that causes stasis of blood flow in the central retinal vein, which then turns into an acute change in pressure of the central retinal artery, and thus may precipitate a hemorrhage.[5,6] Still, not all infants born via vaginal delivery have FH. Therefore, there must be maternal or neonatal factors that remain poorly understood that influence the development of FH at birth.

Little is known about FH at birth because evidence is limited and prospective studies are usually conducted in select populations.[2,7] The studies that have examined FH at birth report that FH are not uncommon at birth, are more frequent among infants delivered via vaginal delivery, and at times can take up to 58 days to resolve completely.[8] No study has performed universal retinal examination on a diverse group of infants such as the United States population. Herein, we present the results of a universal newborn ocular screening initiative conducted in the United States. The study aimed to determine the birth prevalence of FH, to describe risk factors for FH, and to describe the retinal layer, location, characteristics, and laterality of FH. We hypothesized that FH is present in a large proportion of otherwise healthy newborns and that vaginal delivery increased the odds of FH.

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Methods

Study Design

The Newborn Eye Screen Testing (NEST) study was a prospective institutional cohort study conducted at Lucile Packard Children's Hospital (LPCH) at Stanford University School of Medicine. It was designed to determine the birth prevalence of ophthalmic disease and the long-term vision outcomes of newborns with ocular abnormalities identified at birth. Universal newborn screening with retinal image photography was offered to all infants born at LPCH who do not undergo retinopathy of prematurity (ROP) screening. A pediatric vitreoretinal specialist (D.M.M.) reviewed images sent to the Byers Eye Institute telemedicine reading center. Parents were notified within 48 hours of any abnormal screenings. Baseline demographic, maternal, obstetric, delivery, and newborn characteristics were recorded for each subject. In this article, we report the 1-year birth prevalence, characteristics, and associated risk factors for FH among newborns screened in the NEST study during the first year of enrollment.

Ethical Considerations

The Institutional Review Board and Ethics Committee at Stanford University School of Medicine prospectively approved this study (Institutional Review Board no. 25098). Informed consent was obtained from all subjects participating in NEST screening, and the study was conducted in a Health Insurance Portability and Accountability Act (HIPAA)-compliant fashion. All research adhered to the tenets of the Declaration of Helsinki.

Operational Logistics

Lucile Packard Children's Hospital is one of only a few hospitals offering quaternary care in Northern California. It captures an ethnically, geographically, culturally, and socioeconomically diverse patient population. The hospital has 3 levels of newborn care: the well-baby nursery, the intermediate care nursery, and the neonatal intensive care unit. All infants who did not qualify for ROP examination were considered eligible for screening.

At Stanford, a telemedicine infrastructure is in place for the Stanford University Network for the Diagnosis of Retinopathy of Prematurity initiative that screens premature infants for ROP. The NEST study used the same network with a separate database routed to a central reading center at Byers Eye Institute. Infants who did not require ROP screening were offered screening with the NEST study. For those who agreed to participate, images were obtained, stored electronically, and forwarded via a HIPAA-compliant, encrypted, secure image server to the reading center. One pediatric vitreoretinal specialist (D.M.M.) then interpreted these images. Parents were contacted within 48 hours of screening if the examination warranted ophthalmic referral.

Patients and Study Population

Selection of subjects for the study aimed to maximize the study's external and internal validity by using a large, tertiary referral center drawing from an ethnically, racial, and socioeconomically diverse patient population. The target population was all newborns in the United States who were 37 weeks' postmenstrual age or older. The source population was all infants born at LPCH. The eligible population was all infants born at LPCH weekdays excluding holidays who were deemed stable for retinal image photography examination by their attending pediatrician at morning rounds. The study sample represented subjects whose parent and pediatrician consented to the study and who completed the screening procedure.

Inclusion criteria were all live infants born at LPCH who were 37 weeks' postmenstrual age or older from July 25, 2013, through July 25, 2014. Exclusion criteria were patients who were bilaterally anophthalmic, patients whose images or medical charts were not available for review, patients with infectious conjunctivitis (risk of transmission via camera contact lens), and patients deemed too unstable for examination by their attending pediatrician. Informed consent and HIPAA forms included risks, benefits, and alternatives, which were discussed thoroughly with parents before obtaining consent for screening. The consent process was conducted in the parent's preferred language using translators when necessary. The screening was offered free of charge to all parents. For subjects who declined screening, a brief questionnaire about their demographics, delivery method, and reasons for not participating was administered. No standard treatment was withheld or delayed for the purposes of this study.

Photography Protocol

The RetCam III (Clarity Medical Systems, Pleasanton, CA) was used to obtain wide-angle images of all infants enrolled in the NEST study. A neonatal intensive care unit–certified nurse was trained before initiating screening. First, Clarity Medical Systems provided RetCam III training by a certified ophthalmic photographer using both mannequins and live infants. There the nurse was observed and corrected on technique for capturing high-quality images and managing potential adverse outcomes. Second, the nurse was trained by the overseeing vitreoretinal specialist (D.M.M.) to obtain photographs of adequate quality and proper retinal views for physician reading.

Parents and nursing staff assisted in positioning the newborn during screening. Parents were encouraged to swaddle infants and to offer nonnutritive sucking during the examination, and if necessary, nursing staff provided oral sucrose solution to agitated infants before the examination. These interventions have been shown to reduce infant pain profiles during ophthalmic screening.[9,10] Subjects' eyes were dilated with 2.5% phenylephrine and 1% tropicamide 30 to 60 minutes before examination. Feedings were discontinued 2 hours before and after examination, in keeping with aspiration precaution guidelines. Infants were evaluated continuously during the examination for signs of apnea or distress. A topical anesthetic 0.5% proparacaine was administered in each eye before examination. A sterile lid speculum was used to open the eye and provide adequate exposure for photography. To couple the digital camera lens to the infant's cornea, 2.5% hydroxypropyl methylcellulose was used. Digital images were obtained by the nurse and were stored on the RetCam III computer hard drive as well as input into the NEST study telemedicine database management system via automated, HIPAA-compliant synchronization.

The goal was to obtain at least 6 clearly focused images in each eye and 1 external image of the face using the 130° lens (Fig 1A): (1) iris image, (2) optic nerve centered, (3) optic nerve superior, (4) optic nerve inferior, (5) optic nerve nasal, and (6) optic nerve temporal. After screening, the infant was observed by the neonatal intensive care unit nurse for any adverse outcomes. In accordance with the current standard for red reflex screening, all screenings were performed before hospital discharge (mean, 45.0 hours; range, 11.6–103.3 hours). In general at LPCH, newborns are hospitalized for 48 hours after vaginal birth and 72 hours after cesarean section. Therefore, an effort was made to screen newborns within 48 hours after vaginal delivery and within 72 hours after cesarean delivery. The nursing staff did not obtain images during weekends.

Data Collection and Management

Retinal images were reviewed at the Byers Eye Institute telemedicine reading center, and a pediatric vitreoretinal specialist (D.M.M.)