ORIGINAL RESEARCH - PEDIATRIC IMAGING

Intracranial Hemorrhage in Asymptomatic Neonates:

Prevalence on MR Images and Relationship to Obstetric and Neonatal Risk Factors¹

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Purpose:

To retrospectively evaluate the prevalence of neonatal intracranial hemorrhage (ICH) and its relationship to obstetric and neonatal risk factors.

Materials and Methods:

Pregnant women were recruited for a prospective study of neonatal brain development; the study was approved by the institutional review board and complied with HIPAA regulations. After informed consent was obtained from a parent, neonates were imaged with 3.0-T magnetic resonance (MR) imaging without sedation. The images were reviewed by a neuroradiologist with 12 years of experience for the presence of ICH. Medical records were prospectively and retrospectively reviewed for selected risk factors, which included method of delivery, duration of labor, and evidence of maternal or neonatal birth trauma. Risk factors were assessed for relationship to ICH by using Fisher exact test statistics.

Results:

Ninety-seven neonates (mean age at MR imaging, 20.8 days \pm 6.9 [standard deviation]) underwent MR imaging between the ages of 1 and 5 weeks. Eighty-eight (44 male and 44 female) neonates (65 with vaginal delivery and 23 with cesarean delivery) completed the MR imaging evaluation. Seventeen neonates with ICHs (16 subdural, two subarachnoid, and six parenchymal hemorrhages) were identified. Seven infants had two or more types of hemorrhages. All neonates with ICH were delivered vaginally, with a prevalence of 26% in vaginal births. ICH was significantly associated with vaginal birth (P < .005) but not with prolonged duration of labor or with traumatic or assisted vaginal birth.

Conclusion:

Asymptomatic ICH following vaginal birth in full-term neonates appears to be common, with a prevalence of 26% in this study.

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ntracranial hemorrhage (ICH) in full-term neonates commonly is associated with apnea, bradycardia, and seizures (1–4). Subdural, subarachnoid, intraparenchymal, and intraventricular hemorrhages have been identified in symptomatic full-term neonates (5–8). Several factors have been reported to increase the risk of symptomatic ICH in full-term newborns, and these factors include assisted vaginal delivery (forceps or vacuum extraction), maternal parity, fetal weight, and prolonged duration of labor (9–14).

Imaging studies indicate that ICH can occur in asymptomatic newborns (15–17), though precise incidence and distribution of ICH in asymptomatic full-term neonates is not clear. Results of one large prospective study with imaging (18), which was conducted by using a 0.2-T magnetic resonance (MR) imager, indicated that there was an 8% prevalence of subdural hemorrhage in newborns; subdural hemorrhage was associated with vaginal delivery. In the study, all subdural hemorrhages resolved at follow-up imaging 4 weeks later.

While we conducted a prospective study of normal brain development by using a 3.0-T MR imager, we noted several asymptomatic full-term neonates with ICH. We hypothesized that asymptomatic ICH would be associated with vaginal birth, traumatic vaginal birth, and prolonged duration of labor. Thus, the purpose of our study was to retrospectively evaluate the prevalence of neonatal ICH and its relationship to obstetric and neonatal risk factors.

Advances in Knowledge

- Intracranial hemorrhages are common in asymptomatic neonates after vaginal delivery, with an estimated prevalence of 26%.
- Intracranial hemorrhages in asymptomatic neonates delivered vaginally are not associated with overt signs of trauma or with assisted delivery (forceps, vacuum).

Materials and Methods

Patients

Pregnant mothers were recruited from December 2002 to July 2005 as part of an ongoing prospective study about the investigation of prenatal and neonatal brain development. The cohort included control neonates and two groups of neonates at high risk for psychiatric or neurodevelopmental disorders: the offspring of mothers with schizophrenia and neonates diagnosed with fetal isolated mild ventriculomegaly (MVM). Control mothers did not have a history of psychotic illness, and their offspring did not have MVM. Exclusion criteria for all groups in the parent study included major maternal medical illnesses or major congenital abnormalities depicted with ultrasonography at 18-20 weeks gestation. Our ongoing Health Insurance Portability and Accountability Act-compliant study was approved by our institutional review board, and informed consent was obtained from the parents of the neonates. The analysis performed in the retrospective study we report here is considered within the scope of the initially approved research, as has been confirmed by our institutional review board.

Neonates who underwent MR imaging after 5 weeks of age were excluded from the nested case-control analysis, as Whitby et al (18) found that all hemorrhages identified at birth had resolved by that age. Both neonates at high risk for psychiatric or neurodevelopmental disease and neonates without either were included in the analysis, as there is no a priori evidence that such high-risk status confers risk of ICH.

Imaging

Neonates were imaged by using a 3.0-T MR imager (Magnetom Allegra; Siemens Medical Systems, Malvern, Pa) without sedation (19). Neonates were fed, swaddled, fitted with ear protection, and had their heads secured in a vacuum-fixation device. T1-weighted structural pulse sequences were either a three-dimensional magnetization-prepared rapid acquisition gradient-echo

sequence (repetition time msec/echo time msec/inversion time msec, 1820/ 4.38/400; flip angle, 7°) or a two-dimensional spoiled gradient-echo fast low-angle shot sequence (repetition time msec/echo time msec, 15/7; flip angle, 25°). Intermediate-weighted and T2-weighted images were obtained with a turbo spin-echo sequence (6200/20, 119 or 7000/18, 108; flip angle, 150°). Spatial resolution was $1 \times 1 \times 1$ -mm voxel for T1-weighted images and $1.25 \times 1.25 \times 1.5$ -mm voxel with 0.5-mm intersection gap (1 \times 1 \times 3.0-mm voxel with 0.9-mm intersection gap for earliest studies) for intermediate-weighted and T2-weighted images.

A board-certified neuroradiologist (J.K.S.) with 12 years of experience in reading neonatal images retrospectively reviewed all MR images for ICH and was blinded to neonatal and obstetric data. Abnormal areas of signal intensity with signal characteristics compatible with blood products were identified (eg, subacute blood, which was bright on T1weighted images and dark or isointense on T2-weighted images). The location of this area of abnormality determined the classification; for example, a collection between the brain and skull or a dural reflection that did not enter the cortical sulci was considered subdural, one that entered the cortical sulci or cerebrospinal fluid cisterns was considered subarachnoid, and a lesion that was surrounded by brain parenchyma was con-

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Abbreviations:

ICH = intracranial hemorrhage MVM = mild ventriculomegaly

Author contributions:

Guarantors of integrity of entire study, C.B.L., J.K.S., J.H.G.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; manuscript final version approval, all authors; literature research, C.B.L., J.K.S., L.H.M., H.M.W., N.C.C., J.H.G.; clinical studies, J.K.S., L.H.M., J.H.G.; statistical analysis, C.B.L., J.K.S., R.M.H., J.H.G.; and manuscript editing, all authors

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sidered intraparenchymal. Admittedly, there could be some uncertainty as to the exact location of some very small hemorrhages. For example, a small epidural hematoma may be indistinguishable from a small subdural hematoma. In such an instance, the location was assumed to be subdural. Patients were classified as having ICH or not having it on the basis of this reading. Neonates without an adequate T1-weighted image were excluded, as all hemorrhages were identified on the T1-weighted image.

Data Collection

In the protocol for the parent study, one of two trained research associates prospectively collected the following obstetric data: maternal age and ethnicity, whether a cesarean or vaginal delivery had been performed, and whether assisted vaginal delivery (forceps or vacuum) had been performed. Separate sets of medical records were retrospectively reviewed by a medical student (C.B.L.) and a neurosurgery resident (L.H.M.) to obtain information about the duration of labor, duration of ruptured membranes, and maternal trauma. Duration of labor was defined as the length of time between the reported onset of maternal contractions and delivery. Duration of ruptured membranes was defined as the length of time between the rupture of maternal membranes and delivery. Maternal birth trauma was defined as vaginal, labial, or perineal lacerations.

Two trained research associates prospectively collected the following neonatal data: Apgar scores; occurrence of neonatal sepsis, neonatal asphyxia, neonatal apnea, and neonatal seizures; duration of hospital stay; sex; neonatal head circumference; birth weight; gestational age at birth; and gestational age at MR imaging. Two individuals (C.B.L., L.H.M.), who conducted a retrospective chart review by independently reviewing individual sets of records, recorded external evidence of neonatal birth trauma in the form of cephalohematoma, scalp laceration, or bruising associated with the use of forceps.

Statistical Analysis

Neonates were classified by the neuroradiologist (J.K.S.) who read the images in two groups: those with ICH identified on MR images and those without ICH. Binary and categoric obstetric and neonatal variables were compared between the groups by using the Fisher exact test. Group differences in continuous variables, such as duration of labor and duration of ruptured membranes, were compared with the Wilcoxon rank sum test. Data analyses were performed by using statistical software (SAS for Windows, release 9.1; SAS Institute, Cary, NC). A difference with P < .05 (two-tailed test) was considered significant. Because MVM could theoretically increase the risk of ICH, all analyses were performed a second time with exclusion of the cases with MVM.

Results

Patients

One hundred eighteen neonates (mean gestational age at birth, 39.2 weeks; range, 35.1–42.0 weeks) were imaged in the parent study; 97 had undergone MR imaging between the ages of 1 and 5 weeks after birth (mean age at MR imaging, 20.8 days \pm 6.9 [standard devia-

tion]). Nine neonates were excluded from this analysis because a T1weighted sequence was not performed. The final 88 (44 male and 44 female) neonates in our study included 69 control neonates without risk for psychiatric or neurodevelopmental disorders (four from twin pregnancies), 12 neonates with prenatal MVM, and seven offspring of mothers with schizophrenia. Among the 88 neonates, maternal ethnicity was as follows: 69 (78%) were white, 16 (18%) were African American, and three (4%) were Asian American. Mean maternal age was 28.6 years \pm 5.3. In 65 (74%) of neonates, delivery was vaginal; in 23 (26%), delivery was cesarean.

Seventeen (19%)—15 control neonates without a high risk for psychiatric or neurodevelopmental disorders, one neonate with MVM, and one offspring of a mother with schizophrenia—of 88 neonates had ICHs that were clinically silent. The ICHs (Figs 1–3) were observed in 16 neonates with single or multiple subdural hematomas and one neonate with an isolated germinal matrix hemorrhage. Subdural hemorrhage often coexisted with other types of ICH. Two neonates had additional subarachnoid hemorrhages, and five had coexisting intraparenchymal hemorrhages. The

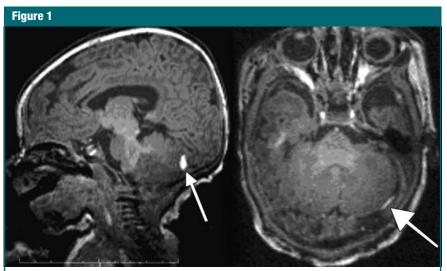


Figure 1: Sagittal (left) and transverse (right) T1-weighted three-dimensional magnetization-prepared rapid gradient-echo MR images (1820/4.38/400; flip angle, 7°; section thickness, 1 mm) in a neonate show typical size and location of subdural hemorrhage (arrow).

intraparenchymal hemorrhages were periventricular (hemorrhagic periventricular leukomalacia) in two neonates, were in the germinal matrix area in two neonates, and were on the brain surface (contusions) in two neonates (Table 1). All subdural hematomas were infratentorial or low in the occipital or temporal

Risk Factors

All 17 hemorrhages occurred in fullterm neonates delivered through vaginal birth and yielded a prevalence of 26% in vaginal births. Since all hemorrhages occurred in vaginally delivered neonates, the neonates born with cesarean delivery were excluded from the subsequent analysis of other obstetric and neonatal risk factors. Vaginal birth was the only significant risk factor associated with ICH (P < .005). Mothers of neonates with ICH were not more likely to have had assisted vaginal delivery or vaginal, labial, or perineal lacerations. Newborns with ICH were not more likely to have had evidence of birth trauma (Table 2). There were no significant differences in the duration of labor or duration of ruptured membranes (Table 3). There was no difference in gestational age at delivery, Apgar score, duration of hospital stay, birth weight, or head circumference between the neonates with vaginal birth who had ICH and those who did not have ICH; neonates with ICH had a significantly younger gestational age at MR imaging than did neonates without ICH (Table 3).

None of the neonates in this study (with or without ICH) had evidence of asphyxia, sepsis, or a seizure. One neonate with ICH had apnea at birth. A clinical MR image depicted an oropharyngeal mass that was clinically determined to be the cause of respiratory distress. With exclusion of MVM, findings in neonates did not significantly change; vaginal birth was still significantly associated with ICH (P = .008, Fisher exact test).

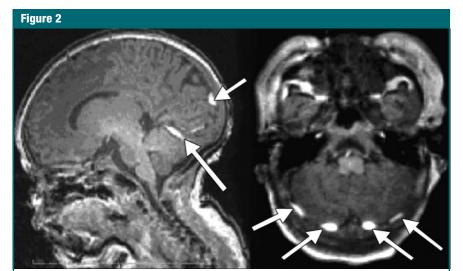


Figure 2: Sagittal (left) and transverse (right) T1-weighted three-dimensional magnetization-prepared rapid gradient-echo MR images (1820/4.38/400; flip angle, 7°; section thickness, 1 mm) in a neonate show the largest infratentorial subdural hemorrhages (arrows) identified.

Discussion

We found that 26% of asymptomatic neonates delivered vaginally had ICH at MR imaging, and this finding suggests that ICH is a fairly common consequence of a normal vaginal delivery. ICH has been thought to be unusual in full-term neonates (1,8,20–27), though the results of this study and those of the study of Whitby et al (28) suggest otherwise.

ICH in full-term neonates often has been associated with birth trauma (6,29–35), which is an association that results from the reporting of hemorrhages identified with cranial imaging in symptomatic neonates in case reports, case series, and case-control studies. In our study, neither assisted vaginal delivery nor evidence of neonatal birth trauma could be used to predict the

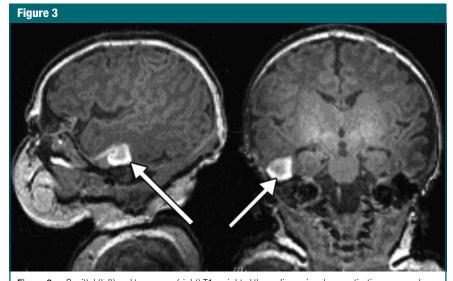


Figure 3: Sagittal (left) and transverse (right) T1-weighted three-dimensional magnetization-prepared rapid gradient-echo MR images (1820/4.38/400; flip angle, 7°; section thickness, 1 mm) in a neonate show intraparenchymal hemorrhage (arrow) in the temporal lobe.

presence of ICH; most (13 of 17, 76%) of the cases of ICH were in the setting of nonassisted vaginal birth. This finding is in agreement with that of Whitby et al (28), who described nine neonates with asymptomatic hemorrhage; in six of the nine neonates, hemorrhage was associated with assisted delivery; in only two of nine neonates with subdural hemorrhages, external birth trauma was an associated finding. The authors concluded that a subdural hematoma was not necessarily associated with obvious birth trauma. Holden et al (16) identified four of 11 neonates with clinically silent ICH; in all, vaginal delivery was uneventful.

The majority of the ICHs in our study were subdural, and most were infratentorial. Subdural hematomas can result from tears in the tentorium, falx, or bridging veins during labor (6,21). Subdural hematoma location may be an important determinant of symptoms, as findings of this study and those of the study of Whitby et al (28) suggest that peritentorial subdural hematomas occur frequently and without immediate clinical consequence. Alternately, even small amounts of subdural hemorrhage in the posterior fossa may lead to obstructive hydrocephalus or neurologic deficits (21).

Subarachnoid, intraparenchymal, and germinal matrix hemorrhages in the full-term neonate previously have been associated with birth trauma (6,36), though the neonates with subarachnoid and intraparenchymal hemorrhages in our study did not have obvious evidence of birth trauma. In a review of seven spontaneous parenchymal and subarachnoid hemorrhages in full-term neonates, Huang and Robertson (7) suggest that open sutures and the compliance of the calvaria lead to shifting of cranial bones during vaginal delivery and, thus, to compression of brain tissue, tearing of the falx or tentorium, or damage of bridging veins, with resulting parenchymal or subarachnoid hemorrhage. Of relevance to the neonate with bilateral anterior temporal contusions in our study, Huang and Robertson (7) note that the pterion is a large "relatively

Table 1				
Description of the ICHs				
Case No.	Туре	Location	No. of ICHs	
1	Subdural, subarachnoid, intraventricular	Posterior fossa, occipital lobe	Multiple	
2	Subdural, parenchymal	Posterior fossa, periventricular	Multiple	
3	Parenchymal	Germinal matrix	Single	
4	Subdural	Posterior fossa, occipital lobe	Multiple	
5	Subdural	Posterior fossa, occipital lobe	Multiple	
6	Subdural	Posterior fossa	Single	
7	Subdural, parenchymal	Posterior fossa, occipital lobe	Multiple	
8	Subdural	Posterior fossa	Multiple	
9	Subdural	Posterior fossa, occipital lobe	Multiple	
10	Subdural	Posterior fossa	Single	
11	Subdural	Posterior fossa	Single	
12	Subdural, parenchymal	Posterior fossa, occipital lobe, periventricular	Multiple	
13	Subdural	Posterior fossa, occipital lobe	Multiple	
14	Subdural, parenchymal	Posterior fossa, occipital lobe, temporal lobe	Multiple	
15	Subdural	Posterior fossa, occipital lobe	Multiple	
16	Subdural, parenchymal	Temporal fossa, germinal matrix	Multiple	
17	Subdural, subarachnoid	Posterior fossa, occipital lobe	Multiple	

Evidence of Traumatic Birth				
	With Hemorrhage	Without Hemorrhage		
Гуре	(n = 17)	(n = 71)	P Value	
Assisted delivery	4 (24)	9 (13)	.28	
Neonatal trauma	1 (6)	8 (11)	>.99	
Maternal lacerations	11 (65)	28 (39)	.1	

unprotected sutural confluence," which makes it a site of injury.

mothers for maternal lacerations. Numbers in parentheses are percentages.

It is important to note that the pattern of ICH in the neonates in our study is different from that found in infants with nonaccidental head injuries. Nonaccidental head injuries typically cause subdural hematomas that are generally located in the interhemispheric fissure or over the cerebral convexities; these hematomas are often, but not always, of differing ages (37). In our study, the subdural hemorrhages were of the same age in all 16 neonates, and the majority of the subdural hemorrhages were in the posterior fossa or over the occipital lobes near the tentorium. The charac-

teristics of such hemorrhages are consistent with previously described birth injuries (18). None of the subdural ICHs were interhemispheric. As MR imaging evaluation of neonates becomes more common in clinical practice, these types of incidental hemorrhages are likely to be identified more frequently. Radiologists and pediatricians must become familiar with the appearance of these hemorrhages and be able to distinguish them from nonaccidental head injuries.

Cranial MR imaging is superior to computed tomography for identification of hemorrhages, especially extracerebral hemorrhages and posterior fossa subdural hemorrhages, in neonates

(38-40). The higher rate of ICH observed in our study compared with the rate in the study of Whitby et al (18) may be related to the improved capability of 3.0-T MR imaging to depict hemorrhages. Whitby et al used low-fieldstrength 0.2-T MR imaging within 48 hours after birth. In the setting of hyperacute hemorrhage, low-field-strength MR imaging may afford good detection because of the T1 contrast (41). Images in our study were obtained 1-5 weeks after delivery. The T1 contrast achieved by using a T1 technique at a higher field strength also may be more sensitive to depiction of subacute hemorrhage, as the increased time allows the hemoglobin to break down to methemoglobin, which is bright on T1-weighted images. All the hemorrhages in our study were dark, if they could be depicted at all, on T2-weighted images. Since the dark hemorrhage was usually adjacent to a normal dark structure, such as the dura or dural sinus, the hemorrhages were not conspicuous on T2-weighted images. Because 3.0-T imaging is becoming more common, our study findings suggest that neonatal ICHs will become increasingly recognized in clinical settings.

There were limitations to our study. The images were not obtained immediately after birth but in weeks 1–5 after

birth, and, perhaps, we missed cases of ICH that had resolved. Neonates with ICH had a younger mean gestational age at MR imaging than did those without ICH, and this finding suggests that images obtained closer to birth may depict ICH more frequently. Also, our imaging protocol did not include T2*-weighted or magnetic susceptibility-weighted images, which might be even more sensitive for depiction of hemorrhage. No follow-up images were obtained to determine imaging resolution of hemorrhage, and no clinical follow-up was performed after the identification of ICH. The protocol in the parent study included neurodevelopmental follow-up and MR imaging follow-up at ages 1 and 2 years, but, to date, follow-up has not been performed in any of the neonates with hemorrhage. Ultimately, we hope to be able to determine whether ICH is associated with later neurodevelopmental problems.

The high prevalence of ICH in our asymptomatic population is important for several reasons. Our findings indicate that vaginal birth may be inherently traumatic to the neonatal brain and can result in a spectrum of ICHs, which include subdural hematomas and subarachnoid, intraparenchymal, and germinal matrix hemorrhages. Holden et al (16) pointed out that retinal hemor-

rhage also is observed in 20%-40% of newborns and that red blood cells often are found in the cerebrospinal fluid of newborns, and these findings indicate that there is trauma after vaginal birth. The long-term consequences of these hemorrhages are unknown at this time, though it is likely that small subdural hemorrhages resolve quickly without substantial consequence.

It is possible, however, that some of these incidental ICHs that occur after vaginal birth may have long-term consequences for subsequent neurocognitive development or may contribute to the development of "idiopathic" epilepsy. These incidental hemorrhages also may increase the risk for complex multifactorial neuropsychiatric disorders such as schizophrenia, which has been associated with perinatal birth complications (42). In addition, ICH may be a marker of traumatic forces that could cause more subtle injury to the developing brain that would not be apparent on MR images; examples of these traumatic forces are transient ischemia or white matter tract damage, which would also affect subsequent neurodevelopment. We plan longitudinal follow-up of this cohort, and the findings from this follow-up may suggest answers to these important questions.

Table 3

Newborn and Labor Variables With Hemorrhage Without Hemorrhage Variable (n = 17)(n = 71)P Value Gestational age at birth (wk) 39.0 (1.0) 39.3 (1.6) .44 Gestational age at MR imaging (wk) 41.4 (1.2) 42.4 (1.7) .02 Apgar score 1 min 8.1 (1.0) 7.8 (1.5) .48 5 min 8.9 (0.4) 8.8 (0.7) .46 Duration of hospital stay (d) 2.5 (1.2) 2.38 (1.5) .82 Data at birth Head circumference (cm) 33.8 (2.1) 34.4 (1.6) .24 Weight (g) 3267.0 (449.5) 3398.2 (501.5) .33 Duration of labor (h)* 5.8 (0.9-22.4) 7.5 (0-22.4) .74 Duration of ruptured membranes (h)* 4.8 (0.2-18.4) 3.5(0-23.5).18

Note.—Data are means. Numbers in parentheses are standard deviations except where indicated otherwise

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