



Prenatal Detection and Outcome of Intracerebral Hemorrhage

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Abstract

Background: Fetal intracranial hemorrhage occurs in about 1/10000 pregnancies and can pose neurological impairments. Intraventricular hemorrhage is the most frequent subtype. Prenatal assessment with neurosonography and MRI are essential to counsel the parents. We aimed to apply a new proposed classification for IVH on MRI and compare it with the classification performed on ultrasound.

Methods: This single-center retrospective study included all consecutive fetuses with ICH between 2005-2023. Prenatal neurosonogram and fetal MRI, maternal characteristics, etiologic factors, pregnancy outcome and postnatal neurological outcomes were recorded. A recent MRI classification was applied.

Results: We identified 48 fetal ICH cases. Ventriculomegaly was in 77 %, the reason for referral. 91.7 % underwent subsequently fetal MRI investigation; revealing abnormalities in 16.3 %, mainly polymicrogyria or cortical malformations. An etiology could be identified in 18 of 48 cases (37.5%). MRI findings were classified according to a recently proposed classification system. Thirty-four patients were included with a mean GA of 31 weeks (+/-3.6 weeks). There was parenchymal involvement in 61.8%. The parenchymal involvement consisted of porencephaly in 50% and having irregular ventricular borders in 23.5%. MRI detected hemosiderin deposits in 67.6%. The central sulcus was involved in 71.4% with parenchymal malformations. Neurological follow-up data were available for 17/22 cases. Neurodevelopmental delay was reported in 7 cases, four children were developing normally, and six children were less than one year old.

Discussion: In our study, 14 cases were graded with parenchymal involvement on NSG, yet on MRI 17 cases illustrated parenchymal involvement with porencephalic cysts. This new MRI classification provided more detailed information on the extent of parenchymal involvement.

Conclusion: This retrospective case series reports on the perinatal mortality and postnatal morbidity with ICH. Diagnosis of IVH is made in the late second or third trimester. Ventriculomegaly was the most common US finding. Prenatal MRI adds additional information to the initial ultrasound in 16.3 % and is likely to be beneficial for parental counseling. An etiology for IVH was found in 37.5%. We report no loss in Grades I and II.

Keywords: MRI; Intracranial hemorrhage; Neurosonography

Abbreviations: ICH: intracranial hemorrhage; IVH: intraventricular hemorrhage; MRI: magnetic imaging resonance; GA: gestational age NSG: neurosonogram; CMV: cytomegalovirus; TOP: termination of pregnancy

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Introduction

More than 25% of extremely low birth weight (ELBW) / very preterm infants will have some degree of IVH identified in the early newborn period [1]. Postnatal IVH is mostly an injury of the immature brain due to bleeding in the germinal matrix, mainly in the sub-ependyma of the lateral ventricles [2]. It may however also develop within the fetal brain. The incidence of fetal ICH remains unclear mainly because fetal and premature birth conditions are not identical. It is estimated at around 1 in 10.000 pregnancies [3-6]. Fetal ICH is often detected late in pregnancy, during the third trimester. It may pose major challenges later in life as some exhibit important neurologic sequelae.

ICH is classified into 2 main groups: intracerebral and extracerebral. The latter is subsequently categorized into intraventricular and infratentorial. Intraventricular hemorrhage (IVH) – the most common subtype of ICH – is further subdivided into four grades depending on their severity according to the Papile classification modified by Volpe [7,8].

Both maternal and fetal risk factors have been linked to fetal ICH such as pre-eclamptic toxemia, hypoxia, seizures, trauma, placental abruption, immune thrombocytopenia, coagulation disorders, vitamin K deficiency, infections and usage of certain drugs (Warfarin, Cocaine). Fetal factors include intra-uterine growth restriction, umbilical cord abnormalities, fetal alloimmune thrombocytopenia, thrombophilia and maternal-fetal or twin-to-twin transfusion. In most cases, however, the exact underlying etiologic mechanism of fetal ICH remains unidentified.

Fetal neonatal alloimmune thrombocytopenia (FNAIT) involves fetomaternal incompatibility for a platelet antigen. Maternal allo-antibodies cross the placenta after which they bind to fetal platelets causing their destruction. Intracranial hemorrhage occurs in up to 50-80% of the FNAIT cases. Diagnosis implies the confirmation of neonatal thrombocytopenia, anti-platelet allo-antibody testing in maternal serum and genotyping of maternal, paternal and child platelet antigens. The severity of FNAIT tends to worsen with subsequent gestation. IVH might also develop as a rare complication of CMV infection. It is hypothesized that CMV may generate small vessel vasculitis of the germinal matrix triggering thrombotic and hemorrhagic events even in the absence of thrombocytopenia

The sonographic diagnosis of fetal ICH might be difficult, especially in more subtle cases. With widespread use of advancing ultrasonography mainly during the third trimester, antenatal detection of IVH has become more achievable. Prenatal diagnosis provides the opportunity to improve

counselling parents regarding the expected prognosis and further management. Hence, recognition of specific ultrasound features and knowledge of their clinical relevance is essential.

Few postnatal studies are available because of prenatal underdiagnosing and most severe cases end in a termination of pregnancy [5,9]. The purpose of our case series is to display an overview of fetal ICH with their main imaging manifestations, the significance of pre-existing risk factors and the correlation to management options and postnatal outcome.

Methods

This is a single-center retrospective study including patients between 2005 and 2023. Multiple pregnancies were excluded from this case series. Maternal age at the time of diagnosis, parity and gestational age were noted as well as the indication at referral. The occurrence of possible maternal or fetal pre-existing risk factors was searched for. Evaluated sonographic features of the bleeding were as follows: site, size and onset of bleeding, its evolution over time, associated ventriculomegaly, porencephaly or leukomalacia and the presence of other intra- or extracerebral malformations. Data were retrieved from the electronic medical file including obstetric and medical history, serological results, infectious diseases, neurosonographic (NSG) images and reports, MRI reports, and pregnancy outcomes.

All NSG examinations were performed on Voluson 730, S10, E8 or E10 platforms (transabdominal RAB6-D 3D probe 2-8MHz; C2-9-D probe 3-9MHz and transvaginal IC5-9-D probe 4-9MHz) (GE HealthCare, Chicago, Illinois).

IVH was categorized based on the classification applied for neonates: Grade I was defined as bleeding restricted to the subependymal area of the germinal matrix. Grade II and III referred to a hemorrhage occupying the lateral ventricle (uni- or bilaterally) without or with ventriculomegaly (>10mm) respectively. Grade IV hemorrhage was diagnosed in case of an extension within the surrounding parenchyma. All neurosonographic examinations were done by experienced fetal medicine specialists.

MRI examinations were performed on a 1.5T MR imaging system (Sonata before 2010 and Aera from 2010 onwards, Siemens, Erlangen, Germany) with 2 small body coils placed adjacent to each other over the maternal abdomen. The routine clinical protocol included a T2 half-Fourier acquisition single-shot turbo spin-echo with steady-state, free precession sequences in the coronal and sagittal plane regarding the mother; a T2 HASTE of the fetal brain in 3 orthogonal planes relative to the fetus; T2 echo planar imaging (added after 2012), T1 turbo spin echo, and diffusion-weighted imaging of the fetal brain in the axial plane (added routinely from

2016 onwards); and T2 HASTE of 3 fetal body planes and a T1 volumetric interpolated breath-hold examination in the coronal plane. During the period starting from 2010 until 2024, the MRI system was routinely updated but image quality was guarded by the MR physics department. The mother was positioned in the supine or left lateral decubitus position. Before September 2015, maternal sedation (flunitrazepam, 0.5 mg orally 20–30 minutes before the examination) was used when the gestational age (GA) was 30 weeks but later this was abandoned. Only one radiologist with >10y expertise in fetal MRI reviewed all images.

MRI was also classified according to the new proposed classification system for fetal intraventricular hemorrhage and periventricular hemorrhagic venous infarction [10].

Postnatal data were collected on neonatal health, neurological outcomes, and educational progress. Prenatal ICH classification was verified with a postnatal workup - either postmortem pathological investigation or transfontanel ultrasound of the newborn - to evaluate the accuracy of antenatal grading.

All patients with severe abnormalities on NSG or MRI are offered the option of TOP in our center.

From 2017 onwards a thrombogenic platform and extensive postmortem examination are added to our investigation list. Lastly, the neurodevelopment outcome was reported after a neurological assessment conducted by a pediatric neurologist using standardized testing Bayley Scales of Infant and Toddler Development, Kaufman Assessment Battery for Children II (BSID-II)

Clinical data was collected in a customised computer database using File Maker Pro version 17 (Clarif, Cupertino, United States). Metric data are described using mean [\pm SD] and range if normally distributed or median and maximum and minimum values for skewed metric or ordinal data. Categorical data are presented as absolute frequencies and percentages.

A P value \leq 5% (P=.05) indicated significant results. Means were compared using a student's t-test. Frequencies were compared using Fisher's exact test. All analyses were performed using Excel Statistics for Windows.

This study was registered under number ML 8404 and approved by the ethical committee of the University Hospital of Leuven, Belgium.

Results

We identified in total 48 cases of fetal ICH comprising 45 intracerebral and three subdural. The intracerebral hemorrhages were intraventricular at origin in 42 cases. Two were cerebellar, and the remaining one was subarachnoid bleeding.

Based on the initial ultrasound, there were 20, 13, 5, and 4 cases of Grade IV Grade III, Grade II and 4 of Grade I respectively.

The mean age of diagnosis was 31 $\frac{3}{7}$ weeks of gestation for the supratentorial cases, and 30 and 18 $\frac{3}{7}$ weeks for the subarachnoid and infratentorial cases respectively. The mean age for diagnosing the subdural cases was 28 weeks.

In 37 out of 48 (77 %) ventriculomegaly was the reason for referral for a more specialized detailed ultrasound. Two cases of fetal cardiocographic abnormalities were the cause of an extra ultrasound scan. Two patients were referred for intra-uterine growth restriction. Another one was referred because of an echogenic plexus choroideus. Only one case was referred upon the suspicion of an ICH. A cystic region possibly resembling a small remnant of an old hematoma was accidentally noticed at the left cerebellar hemisphere whilst checking a fetus for thyrotoxicosis in a patient with Graves' disease. Only three cases were picked up as intracranial bleeding during routine third-trimester screening. The two infratentorial cases with bleeding in the posterior fossa were due to a Parvo B19.

All but three cases underwent sequential fetal MRI investigation. One MRI was cancelled because of fetal demise. (44/48 cases= 91.7 %). MRI showed additional value in a more precise evaluation of the brain for underlying cerebral developmental abnormalities in 7 cases (16 %) such as polymicrogyria or cortical malformation. On top of that, it also proved to be useful in adequately detecting the presence of intraparenchymal bleeding, porencephaly or leukomalacia, especially in those cases where ultrasound imaging fails short. Two grade IV cases appeared to be ischemic lesions.

The evolution of the ICH was monitored by serial ultrasound in the non-TOP cases. One of them showed progressive ventriculomegaly over time suggestive of aqueduct stenosis. One case of IVH Grade III presented at first with bilateral dilatation of the lateral ventricles, though improved over time with even normalization of the right lateral ventricle size. Remnants of old blood clots were still seen.

We retrieved 4 cases of Grade I IVH. (Table 1) One case was a second-trimester CMV seroconversion leading to subependymal bleeding. In two other cases Beta thalassemia and anti GPIIbIIIa antibodies were the etiologic factors. In one case no etiology was found. Neurologic outcome was normal in 3 out of 4 children. Bailey scores were normal at the age of 2 years in 2 children and normal in the third one at the age of 5 months postnatally. One case was lost for follow-up.

Table 1: Distribution of the 48 cases of the fetal ICH

Type	Gr I	Gr II	Gr III	Gr IV	SD	SA	PF
N=	4	5	13	20	3	1	2
Etiology	03-Apr	03-May	Feb-13	Apr-20	03-Mar	01-Jan	02-Feb
Outcome	2/4 normal Bailey @2y ¼ normal@ 5m ¼ lost FU	2/5 normal but<1 y age 2/5 high morbidity 1/5 lost FU	1 regression to Gr1 4/13 TOP 5/13 neurological impairment 3 to early (3 Months 2/3 VP drain)	18/20 TOP 1 fetal demise @ W34 1/20 lost FU	2 TOP 1NND @d5	Normal Bailey @2y	1 TOP 1 normal Bailey@6 y

Legend:

Gr I: Grade 1 hemorrhage
Gr II: Grade 2 hemorrhage
Gr IV: Grade 4 hemorrhage
SD: Subdural hemorrhage
SA: Subarachnoid hemorrhage
PF: posterior fossa
FU: follow-up
TOP: Termination of pregnancy
Y: year
VP: ventriculoperitoneal

Grade II was diagnosed in 5 children. In a fetus with a Grade II intraventricular hemorrhage, initially, a clot was detected in the third ventricle. Progressively ventriculomegaly developed. A vascular malformation in the choroid plexus was diagnosed. Ventriculoperitoneal shunting (VP Shunting) was performed in the neonatal period. In the other Grade II cases, a mild ventriculomegaly was diagnosed. Postnatal hydrocephaly required a VP shunting after six weeks. At the age of 3 years, a coincidental diagnosis of meningioma was made. At the age of 5 years, a visual impairment (strabismus) was present. In a third case, platelet antibodies were diagnosed. This child had a normal neurologic examination at 7 months of age. In the remaining 2 cases etiologic examination was negative and the neurologic examination was normal at five months of age in one child, the last case was lost for follow-up.

In all cases of Grade III bleeding severe bilateral ventriculomegaly (>15 mm) was diagnosed antenatally. Of the 4 patients that underwent TOP, a possible cause was found in 2 cases: 1 baby was a carrier of factor V Leiden and in another one, WES showed a mutation of the SLC17A gene leading to a free Sialic acid storage disease. Alloimmune thrombocytopenia and TORCH screening were negative in all the other cases. The first surviving child had a bleeding in the basal ganglia and at the age of 42 months, he was developing normally but had a speech delay.

The second child had left hemiplegia at the age of 8 years and went to a regular school. The third child had a disruption of the cavum septi pellucidi and has no Probst Bundles. Postnatally psychomotor retardation and epilepsy developed. The fourth child had a normal psycho-motoric development at the age of 23 months and developed epilepsy seizures at 42

months of age. Finally, the last child required a VP shunt at 3 months of age and had loss of white matter, and visual and motoric impairment at 6 months of age. Two others received a VP drain postnatally and the first neurologic examination at 3 months of age was normal. Finally, 1 child had a normal neurologic examination at 3 months postnatally. One Grade III regressed to Grade I.

Of the 20 Grade IV cases one ended in a fetal demise at 34 weeks of gestation, and one child was lost to follow-up. The remaining 18 pregnancies underwent termination of pregnancy after parental request. An aetiology was found in 4 cases: 2 cases were CMV-related, 1 case with a small deletion on chromosome 9 (GLDC gene) and in one mother we found Factor V Leiden.

The 2 cases with bleeding in the posterior fossa were due to a Parvovirus B19 infection. Diagnosis was made early (17 and 20 weeks of gestation). Their peak systolic velocity was increased to 50 cm/s (> 1.5 Mom for gestational age). Due to liquefaction of the cerebellum one pregnancy ended in a TOP. In the other pregnancy intra-uterine transfusion was carried out and the outcome was normal. The child is doing well at the age of 6 years. Of the 3 cases of subdural bleeding, 2 underwent TOP and 1 child died day 5 postnatally.

In one child Factors 8 and 5 were low where COL4A1 and COL4A2 were normal. In the second case, a coagulopathy was diagnosed with mutations in Coll/EPI 87 and the COLL/ADP 66s. Finally, in the last case, we found Factor V gene mutations. DNA of the fetus was compound heterozygous.

An aetiologic cause for fetal ICH could be identified in 18 of 48 cases (37.5 %). An underlying vascular malformation was detected by antenatal fetal MRI. The placental evaluation discovered a placental disorder resulting in intra-uterine growth restriction and presumably secondary ischemic periventricular germinal matrix bleeding. One pregnancy was severely compromised by a CMV fetopathy. One patient had polytrauma after a train crash including multiple pelvic fractures and lung contusion. Another patient was the victim of domestic violence. One case was potentially caused by an accidental fall on the abdomen. Thrombocyte dysfunction could not be ruled out in 2 of the cases. Factor V deficiency, an autosomal recessive clotting disorder was found in two

children congenitally born with ICH. In the majority of cases (61.7 %) however pre-existing risk factors were not withheld.

FNAIT was only once the causative factor in our case series. A thrombogenic panel introduced in 2017 did not reveal additional information in 0/7 examinations.

In total 25 cases opted to terminate the pregnancy. One fetal demise occurred at week 34. Twenty-two pregnancies ended in a life birth. Parents who desired a postnatal palliation because of an expected unfavorable outcome were advised to pursue a vaginal birth without fetal surveillance. One neonate passed away on day 5 postnatally. 4/48 (8.3 %) children were lost for follow-up.

Neurological follow-up data were available for 17/22 cases (77.3%). Neurodevelopmental delay was reported in 7 cases, four children were developing normally, and six children were less than one year old.

MRI was also classified according to a recently proposed classification system for fetal intraventricular hemorrhage and periventricular hemorrhagic venous infarction. (Table 2)

Thirty-four patients were included with a mean GA of 31 weeks (+/-3.6 weeks). On NSG, three fetuses scored grade I (8.8%), 5 grade II (14.7%), 12 fetuses with grade III (35.3%) and 14 cases with grade IV (41.2%). On MRI, 3 fetuses (8.8%) had no, 6 (17.6%) borderline, 4 (11.8%) mild and 21 (61.8%) severe ventriculomegaly. There was parenchymal involvement in 21 fetuses (61.8%). The parenchymal involvement consisted of porencephaly in 17 (50%) and having irregular ventricular borders in 8 (23.5%). MRI detected hemosiderin deposits in 23 fetuses (67.6%). The central sulcus was involved in 15 fetuses (71.4%) with parenchymal involvement.

Table 2: Findings at MRI

Presence and extent of intraventricular blood		
Ventriculomegaly		N=35
	Normal (<10 mm)	N=7
	Borderline (10 mm - <12 mm)	N=7
	Mild (12- <15 mm)	N=4
	Severe (>15 mm) / hydrocephalus	N=24
Parenchymal hemorrhage /sequela of parenchymal hemorrhage		
Parenchymal hemorrhage	Y/N	22/19
Parenchymal loss		
	Irregular ventricular border	8

	Porencephalic cyst	16
	None	14
Parenchymal hemosiderin deposit*	Y/N	24/17
Location of parenchymal involvement		
Frontal (Right/Left)		Sep-13
	With/without involvement of the central sulcus*	Mar-19
Parietal (Right/Left)		09-May
	With/without involvement of the central sulcus*	06-Aug
Temporal (Right/Left)		04-Jan
Occipital (Right/Left)		02-Feb
	With/without involvement of the visual cortex and/or optic radiation*	0/0
lentiform nucleus (Right/Left)		01-Jan
Thalamus (Right/Left)		
	With/without internal capsule involvement*	0/0
Associated Findings		
Sub-arachnoid involvement		
	Enlargement	1
	Hemorrhage	6
	Effacement (susp. Hydrocephalus)	16
	None	18
Posterior fossa hemorrhage		
	None	28
	Parenchymal one hemisphere	1
	Parenchymal two hemispheres	1
	Parenchymal vermis	0
	Pericerebellar	9
	Cisterna magna	2
* Can be diagnosed only by MRI		

Comparison with existing literature

Literature reports only a few case-control studies where FNAIT, maternal trauma and cerebellar bleeding were examined. All other, either prospective or retrospective studies fail to identify risk factors in half of the cases. (TABLE 3)

Table 3: Our data compared to the literature.

Study	Type study	ICH (N=)	Etiology found (%)	ICH type	Follow-up
Folkerth et al. 2001 (11)	Retro CS	3	15%	IVH(15) SD(2) Complex (3)	1 case 24 months
Strigini et al. 2001 (12)	Retro CS	5	100% (maternal trauma)	Subependymal (1) Hemorrhagic cyst (1) IVH (1) Complex (2)	6-12 months
Ghi et al. 2003 (6)	Retro CS	14	42.8 %	IVH Gr 2 (4) gr 3 (4) gr 4 (3) Infratentorial (2) Subdural (2)	1-48 months (mean 11.6)
Ozduman et al. 2004 (13)	Retro CS	4	0%	IVH (1) supendymal (1) Complex (2)	3-39 months
Elchalal et al. 2005 (5)	Retro CS	29	7.4 %	SD (1) IVH Gr 2 (5) Gr 3 (3) intraparenchymal (6) subependymal (3) cerebellar (1) complex (4) other (5)	30-48 months
Huang et al. 2006 (14)	Retro CS	3	66.6 %	IVH Gr 3 (1) Intraparenchymal (1) choroidal (1)	1 case 20 months
Morioka et al. 2006 (15)	Retro CS	5	0%	IVH Gr 3 (1) Gr 4 (4)	9 moths to 8 years
Luciano et al. 2007 (16)	Prospective cohort	6	33.3 %	IVH Gr 3 (2) Gr 4 (4)	Mean 24 months
Manganaro et al. 2012 (17)	Retro CS	14	7.1 %	IVH (7) intraparenchymal (1) cerebellar (1) complex (3) dural sinus malformation (2)	Not stated
Tiller et al. 2013 (18)	Retro cohort	43	100%	FNAIT (43)	Up til discharge
Kutut et al. 2014 (19)	Retro cohort	6	33.3 %	IVH Gr 4 (1) intraparenchymal (3) complex (2)	6-15 months (median 9.4)
Martino et al. 2016 (20)	Retro CS	17	11.7 %	Cerebellar (17)	24-104 months Mean 53
Tavil et al. 2016 (21)	Retro CS	6	0 %	IVH Gr 3(1) Gr 4 (4) intraparenchymal	0.2- 108 months mean 42.8
Abdelkader et al. 2017 (22)	Prospect CS	20	15%	SD (2) IVH (15) Complex (3)	No follow-up
Maisonneuve et al. 2019 (23)	Retro cohort	4	100%	Cerebellar (4)	Range 3-30 months
Adiego et al. 2019 (24)	Retro CS	14	0%	IVH Gr2 (2), Gr 3 (3), Gr 4 (7) Complex (2)	3-96 months median 28 months
Gupta et al. 2023 (25)	Retro CS	57	8.7 %		1.8 years
Our study 2024	Retro CS	48	37.5%	IVH Gr1 (4), Gr 2 (5), Gr 3 (13), Gr 4 (20), SD (3), SA (1), cerebellar (2)	3-96 months

Discussion

Fetal intracranial hemorrhage (ICH) may occur within the cerebral ventricles, subdural space, or intratentorial. The diagnosis is usually made late in pregnancy, during the third trimester, often after a normal 20-week anomaly scan. Intraventricular hemorrhage (IVH) is the most common subtype, and it is linked to the structural features of the germinal matrix (GM). The GM is a brain region located underneath the ependyma of the lateral ventricles and is mainly composed of neuronal and glial precursor cells. Its vasculature is highly fragile and uniquely susceptible to ischemic injury due to rapid angiogenesis. Bleeding typically originates in the vascular connections between the GM and the subependymal venous network and they are only distinctly detectable after twenty weeks of gestation. Therefore, we plea for a systematic introduction of a third-trimester ultrasound scan, since most cases of IVH are discovered in the late second and third trimesters [26]. Papile classification is based on the localisation of the IVH in association with the presence or absence of ventricular dilatation. The Volpe classification on the other hand is based on the amount of intra-ventricular blood on the parasagittal view of the lateral ventricle combined with the presence of periventricular hemorrhagic infarction of the parenchyma.

ISUOG guidelines recommend an assessment of the symmetry of the hemispheres, the width of the lateral ventricles and an assessment of the parenchyma and cerebellar cortex [27]. In our case study, 76.6 % of referrals were ventriculomegaly, only 1 case was referred for IVH, while three out of 48 were detected by the routine third-trimester scan (8.3 %).

Monogenetic disorders in IVC are described [28,29] We identified genetic anomalies in 38.9 % of cases. WES can increase the diagnostic yield [30].

A subdural hemorrhage (SDH) refers to bleeding outside the brain between the dura and arachnoid mater. It has been associated with trauma to the maternal abdomen. The external impact can cause stretching and tearing of the bridging veins in the subdural space. According to a systematic literature search of Cheung et al. 78% of prenatal cases of SDH are diagnosed after 24 weeks. The mean gestational age in our series was 28 weeks [31]. All SDH in our series were due to a coagulation disorder.

Hayashi et al. noticed that most prenatal cerebellar hemorrhage happen between 21 to 25 weeks of gestation. Both cases were due to Parvovirus B19 -infection and were diagnosed around 18 weeks [32]. Only one of our cases had FNAIT.

The groups of Capasso [33] and Suksumek [34] both reported a case of a neonate with congenital CMV infection and IVH in the occurrence of a normal platelet count and

coagulation profile without restricted growth. Toxoplasmosis and Parvovirus B19 have also been proposed as other causative infective agents.

A blunt prenatal trauma to a maternal abdomen is another mechanism that can lead to fetal ICH with a presumed relatively higher occurrence of the subdural anatomical location.

The systematic review of Joseph et al. detected 13 cases of SDH after either a motor vehicle accident or an assault [35]. Ghi et al. investigated 109 cases of antenatally diagnosed ICH of which 89 were intraventricular and 20 subdural [6]. An earlier abdominal impact was proclaimed in 10 cases of which 2 were subdural versus 8 intraventricular.

Fetal MRI is a safe imaging technique providing high resolution of fetal anatomy. The sonographic visualization of fetal ICH might be compromised by maternal habitus, oligohydramnios.

The sonographic appearances of fetal ICH are extremely variable depending on the location of the bleeding and the timing of the ultrasound. An initial hemorrhage might expand from its location of origin and start to exert pressure on the adjacent tissue.

An IVH arising from the GM might disintegrate the underlying ependyma and further extend into the lateral ventricles. Blood clots obstructing the Sylvian aqueduct will additionally enhance the development of ventriculomegaly. Severe hydrocephalus will lead to cortical thinning and inhibit proper cerebral growth and evolution. A significant hemorrhage might even breach and occupy the surrounding brain parenchyma itself. The grading classification of IVH is based on the different stages of this process. A significant mass effect from a large SDH could lead to a midline shift of the falx cerebri. Rising intracranial pressure either due to an expanding hemorrhage volume or major hydrocephalus may cause macrocephaly. An acute bleed presents as an echogenic zone on ultrasound whereas a chronic hematoma appears more heterogenic or sonolucent. The transitional stage is characterized by mixed echogenicity because of gradual breakdown and liquefaction. A mixed irregular echogenic mass may also be seen when acute bleeding originates within a pre-existing chronic hemorrhage site. engaged fetal head and increased cranial ossification in the third trimester of pregnancy. Nowadays hemosiderin deposit is easily picked up by MRI. In our study, MRI gave additional information to prenatal ultrasound in 16.27 % of the cases; 14 cases were graded with parenchymal involvement on NSG, yet on MRI 17 cases illustrated parenchymal involvement with porencephalic cysts. Also, our data demonstrates a difference between the old classification and the new classification by providing more detailed information on the extent of parenchymal involvement which might hold important

information for parental counselling. Due to the retrospective nature, we were not able to apply this new classification on NSG nor examine all fetuses with diffusion-weighted imaging.

Neurologic outcome

Little data exists regarding neurodevelopmental outcomes in the case of prenatal ICH. Dunbar et al. reported an occurrence of motor impairment in 7.7 %, but this was the only surviving child out of 13 cases of Grade I and II, and the severity was not reported [36]. The association with high-grade IVH has a poor neurologic prognosis. The exact location of bleeding, laterality, midline shift, and the involved areas involved may influence motor and cognitive impairments. Anterior frontal and temporal parenchymal involvement increase risks of cognitive and behavioral sequelae. Frontoparietal and trigonal involvement are associated with motor impairment [37,38].

The substantial literature review of 93 cases by Ghi et al. outlined a rather poor prognosis with antenatal ICH in general with nearly 40% mortality either in utero or within the first month after birth. Among the survivors, more than 50% displayed neurodevelopmental delays at short-term follow-up [6]. The outcome of fetal IVH was highly associated with the grade of the bleeding. Grade I has a fairly good outcome. Grade I to II lesions might even resolve over time and usually go along with an excellent outcome. Grade III IVH has been associated with a higher rate of moderate to severe neurological deficits. Furthermore, progression from a lower to a higher-grade hemorrhage is possible which seems to be associated with a worsened prognosis. Significant hydrocephaly or important hemorrhagic mass effect leading to cortical thinning appears to be a dismal prognostic factor.

Children with prenatal cerebellar hemorrhagic disruption are at risk for impaired motor function, weakened cognition and social behavioral deficits such as autism spectrum disorders.

The optimal delivery mode of an infant diagnosed with fetal ICH needs to be determined. If a bad outcome is anticipated due to the appearance of severe lesions, conservative management consisting of a vaginal delivery without cardiotocographic surveillance may be proposed. Whether a caesarean section might improve the outcome of children with less serious lesions is not completely understood. Caesarean delivery might however be indicated in case of increased risk of dystocia due to enlarged fetal head diameters. It should also be considered to minimize the hemorrhagic risks when there is evidence of high susceptibility for fetal bleeding such as in allo-immune thrombocytopenia or certain coagulopathies. Patients should be encouraged to undergo further diagnostic work-up either after live birth or termination of pregnancy.

Strengths and Limitations

The strength of this study lies in the large group of patients with a substantial amount of live births. In addition, almost all included patients received a prenatal MRI, allowing to include the evaluation of the novel MRI-based scoring system. Another strength is the long follow-up of these children compared to literature. Using this MRI-based scoring system in counselling parents regarding neurologic outcomes will be the subject of further research.

Limitations the retrospective character of the study. Few of the patients were lost for follow-up

Conclusion

This retrospective case series reports on the perinatal mortality and postnatal morbidity of fetuses with ICH. Ventriculomegaly was the most common US finding for referral. Prenatal MRI adds to the initial ultrasound in 16.27 %. An etiology for IVH was found in 38.9 %. Neurologic follow-up, ranging from 3 to 96 months, was documented in 77.3 % of cases. A novel MRI-based scoring system to evaluate neurologic outcomes may improve prenatal assessment of fetal IVH. Given the more extensive description of parenchymal involvement, but needs further investigation.

References

1. Sherlock R, Anderson P, Doyle L; Victorian Infant Collaborative Study Group. Neurodevelopmental sequelae of intraventricular hemorrhage at 8 years of age in a regional cohort of ELBW/very preterm infants. *Early Hum Dev* 81 (2005): 909-916.
2. Del Bigio M. Cell proliferation in human ganglionic eminence and suppression after prematurity-associated haemorrhage. *Brain* 134 (2011): 1344-1361.
3. Dunbar M, Kirton A. Perinatal Stroke. *Semin Pediatr Neurol* 32 (2019): 100767.
4. Dunbar MJ, Woodward K, Leijser LM, et al. Antenatal diagnosis of fetal intraventricular haemorrhage: systematic review and meta-analysis. *Dev Med Child Neurol* 63 (2021): 144-155.
5. Elchalal U, Yagel S, Gomori JM, et al. Fetal intracranial haemorrhage (fetal stroke): does grade matter? *Ultrasound Obstet Gynecol* 26 (2005): 233-243.
6. Ghi T, Simonazzi G, Perolo A, et al. Outcome of antenatally diagnosed intracranial haemorrhage: case series and review of the literature. *Ultrasound Obstet Gynecol* 22 (2003): 121-30.
7. Papile LA, Burstein J, Burstein R, et al. Incidence and evolution of subependymal and intraventricular haemorrhage: a study of infants with birth weights less than 1,500 gm. *J Pediatr* 92 (1978): 529-34.

8. Volpe JJ. Intraventricular haemorrhage and brain injury in the premature infant. Diagnosis, prognosis, and prevention. *Clin Perinatol.* 16 (1989): 387-411.
9. Sileo FG, Zöllner J, D'Antonio F, et al. Perinatal and long-term outcome of fetal intracranial haemorrhage: systematic review and meta-analysis. *Ultrasound Obstet Gynecol* (2022): 585-595.
10. Hadi E, Haddad L, Levy M, et al. Fetal intraventricular haemorrhage and periventricular hemorrhagic venous infarction: time for dedicated classification system. *Ultrasound Obstet Gynecol* 64 (2024): 285-293.
11. Folkerth RD. Germinal matrix haemorrhage: destroying the brain's building blocks. *Brain.* 134 (2011): 1261-1263.
12. Strigini FA, Cioni G, Canapicchi R, et al. Fetal intracranial haemorrhage: is minor maternal trauma a possible pathogenetic factor? *Ultrasound Obstet Gynecol* 18 (2001): 335-342.
13. Ozduman K, Pober BR, Barnes P, et al. Fetal stroke. *Pediatr Neurol.* 30 (2004): 151-162.
14. Huang YF, Chen WC, Tseng JJ, et al. Fetal intracranial haemorrhage (fetal stroke): report of four antenatally diagnosed cases and review of the literature. *Taiwan J Obstet Gynecol* 45 (2006): 135-141.
15. Morioka T, Hashiguchi K, Nagata S, et al. Fetal germinal matrix and intraventricular haemorrhage. *Pediatr Neurosurg* 42 (2006): 354-361.
16. Luciano R, Baranello G, Masini L, et al. Antenatal post-hemorrhagic ventriculomegaly: a prospective follow-up study. *Neuropediatrics* 38 (2007): 137-142.
17. Manganaro L, Bernardo S, La Barbera L, et al. Role of foetal MRI in the evaluation of ischaemic-haemorrhagic lesions of the foetal brain. *J Perinat Med* 40 (2012): 419-426.
18. Tiller H, Kamphuis MM, Flodmark O, et al. Fetal intracranial haemorrhages caused by fetal and neonatal alloimmune thrombocytopenia: an observational cohort study of 43 cases from an international multicentre registry. *BMJ Open.* 3 (2013): e002490.
19. Kutuk MS, Croisille L, Gorkem SB, et al. Fetal intracranial haemorrhage related to maternal autoimmune thrombocytopenic purpura. *Childs Nerv Syst* 30 (2014): 2147-2150.
20. Kutuk MS, Croisille L, Gorkem SB, et al. Fetal intracranial haemorrhage related to maternal autoimmune thrombocytopenic purpura. *Childs Nerv Syst* 30 (2014): 2147-2150.
21. Tavil B, Korkmaz A, Bayhan T, et al. Foetal and neonatal intracranial haemorrhage in term newborn infants: Hacettepe University experience. *Blood Coagul Fibrinolysis* 27 (2016): 163-168.
22. Abdelkader MA, Ramadan W, Gabr AA, et al. Fetal intracranial haemorrhage: sonographic criteria and merits of prenatal diagnosis. *J Matern Fetal Neonatal Med.* 30 (2017): 2250-2256.
23. Maisonneuve E, Ben M'Barek I, Leblanc T, et al. Managing the Unusual Causes of Fetal Anemia. *Fetal Diagn Ther.* 47 (2020): 156-164.
24. Adiego B, Martínez-Ten P, Bermejo C, et al. Fetal intracranial haemorrhage. Prenatal diagnosis and postnatal outcomes. *J Matern Fetal Neonatal Med* 32 (2019): 21-30.
25. Gupta V, Schlatterer SD, Bulas DI, et al. Pregnancy and Child Outcomes Following Fetal Intracranial Hemorrhage. *Pediatr Neurol.* 140 (2023): 68-75.
26. Drukker L, Bradburn E, Rodriguez GB, et al. How often do we identify fetal abnormalities during routine third-trimester ultrasound? A systematic review and meta-analysis. *BJOG.* 128 (2021): 259-269.
27. Khalil A, Sotiriadis A, D'Antonio F, et al. ISUOG Practice Guidelines: performance of third-trimester obstetric ultrasound scan. *Ultrasound Obstet Gynecol.* 63 (2024): 131-147.
28. Mullaart RA, Van Dongen P, Gabreëls FJ, et al. Fetal periventricular hemorrhage in von Willebrand's disease: short review and first case presentation. *Am J Perinatol.* 8 (1991): 190-192.
29. Ellestad SC, Zimmerman SA, Thornburg C, et al. Severe factor V deficiency presenting with intracranial haemorrhage during gestation. *Haemophilia* 13 (2007): 432-434.
30. Hausman-Kedem M, Malinger G, Modai S, et al. Monogenic Causes of Apparently Idiopathic Perinatal Intracranial Hemorrhage. *Ann Neurol.* 89 (2021): 813-822.
31. Cheung KW, Tan LN, Seto MTY, et al. Prenatal Diagnosis, Management, and Outcome of Fetal Subdural Haematoma: A Case Report and Systematic Review. *Fetal Diagn Ther* 46 (2019): 285-295.
32. Hayashi M, Poretti A, Gorra M, et al. Prenatal cerebellar haemorrhage: fetal and postnatal neuroimaging findings and postnatal outcome. *Pediatr Neurol.* 52 (2015): 529-534.
33. Capasso L, Coppola C, Vendemmia M, et al. Severe fetal intracranial haemorrhage: Congenital Cytomegalovirus infection may play a role? A case report and review of literature. *IDCases.* 25 (2021): e01188.

34. Suksumek N, Scott JN, Chadha R, et al. Intraventricular haemorrhage and multiple intracranial cysts associated with congenital cytomegalovirus infection. *J Clin Microbiol* 51 (2013): 2466-2468.
35. Joseph JR, Smith BW, Garton HJ. Blunt prenatal trauma resulting in fetal epidural or subdural hematoma: case report and systematic review of the literature. *J Neurosurg Pediatr.* 19 (2017): 32-37.
36. Dunbar MJ, Woodward K, Leijser LM, et al. Antenatal diagnosis of fetal intraventricular haemorrhage: systematic review and meta-analysis. *Dev Med Child Neurol.* 63 (2021): 144-155.
37. Bassan H, Limperopoulos C, Visconti K, et al. Neurodevelopmental outcome in survivors of periventricular hemorrhagic infarction. *Pediatrics.* 120 (2007): 785-792.
38. Cizmeci MN, Khalili N, Claessens NHP, et al. Assessment of Brain Injury and Brain Volumes after Posthemorrhagic Ventricular Dilatation: A Nested Substudy of the Randomized Controlled ELVIS Trial. *J Pediatr.* 208 (2019): 191-197.e2.



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