Foetal and neonatal intracranial haemorrhage in term newborn infants: Hacettepe University experience

Betül Tavil[a], Ayşe Korkmaz[b], Turan Bayhan[a], Selin Aytaç[a], Sule Unal[a], Baris Kuskonmaz[a], Sule Yigit[b], Mualla Cetin[a], Murat Yurdakök[b] and Fatma Gumruk[a]

In this study, we aimed to evaluate the incidence, risk factors, causes and clinical management of intracranial haemorrhage (ICH) diagnosed during foetal life or in the first month of life in term neonates with a discussion of the role of haematological risk factors. This study included term neonates (gestational age 37–42 weeks) with ICH diagnosed, treated and followed up in the Neonatal Intensive Care Unit of Hacettepe University, Ankara, Turkey, between January 1994 and January 2014. Medical follow-up was obtained retrospectively from hospital files and prospectively from telephonic interviews and/or clinical visits. During the study period, 16 term neonates were identified as having ICH in our hospital. In six (37.5%) neonates, ICH was diagnosed during foetal life by obstetric ultrasonography, and in 10 (62.5%) neonates, it has been diagnosed after birth. Haemorrhage types included intraventricular haemorrhage (IVH) in eight (50.0%), intraparenchymal haemorrhage in six (37.5%), subarachnoid haemorrhage in one (6.2%) and subdural haemorrhage in one (6.2%) neonate. IVH was the most common ($n = 5/6$, 83.3%) haemorrhage type among neonates diagnosed during foetal life. Overall, haemorrhage severity was determined as mild in three (18.7%) neonates, moderate in three (18.75%) neonates and severe in 10 (62.5%) neonates. During follow-up, one infant was diagnosed as afibrinogenemia, one diagnosed as infantile spasm, one cystic fibrosis, one orofaciodigital syndrome and the other diagnosed as Friedrich ataxia. Detailed haematological investigation and search for other underlying diseases are very important to identify the reason of ICH in term neonates. Furthermore, early diagnosis, close monitoring and prompt surgical interventions are significant factors to reduce disabilities.

Blood Coagulation and Fibrinolysis 2016, **27**:163–168

Keywords: haematological risk factors, intracranial haemorrhage, term neonates

[a]Pediatric Hematology Unit and [b]Neonatal Intensive Care Unit, Faculty of Medicine, Hacettepe University, Ankara, Turkey

Correspondence to Dr Betul Tavil, Hacettepe University Faculty of Medicine, Ihsan Dogramaci Children's Hospital, Pediatric Hematology Unit, Sihhiye, Ankara 06100, Turkey
Tel: +090 312 3051172; e-mail: tavil@hacettepe.edu.tr

Received 30 March 2015 **Revised** 29 June 2015
Accepted 3 July 2015

Introduction

Intracranial haemorrhage (ICH) is mostly a disease associated with prematurity and it is rarely seen in term newborn infants. In the English literature, only case reports and small case series have been reported about ICH in term newborns [1–8]. ICH in term newborn infants has different characteristics from those seen in preterm neonates. It has been suggested that ICH is closely related to mechanical damage such as birth injury, perinatal hypoxic-ischemic events and coagulation disorders in term infants, although it is associated with immaturity of vascular tissues including germinal matrix of ventricles in preterm infants. The anatomical locations of ICH also differ between term and preterm neonates. Intraventricular and periventricular haemorrhage is more frequent in preterm infants, whereas subdural or subarachnoid haemorrhage is usually seen in term neonates [1–8].

Some haematological diseases or underlying disorders may contribute to the development of ICH in term neonates. In this study, we aimed to retrospectively evaluate the incidence, risk factors, causes and clinical management of ICH diagnosed during foetal or the first month of life in term newborns. The role of haematological risk factors will also be discussed.

Materials and methods

This study included term neonates (gestational age 37–42 weeks) with ICH diagnosed, treated and followed up in the Neonatal Intensive Care Unit of Hacettepe University Ihsan Dogramaci Children's Hospital, Ankara, Turkey, between January 1994 and January 2014. Term neonates with ICH diagnosed during foetal life by obstetric ultrasonography or in the first month of their life were identified retrospectively on the basis of hospital records. The demographic and clinical characteristics of all the infants were noted from hospital files and electronic data. The diagnosis of ICH was confirmed by cranial imaging methods, including cranial ultrasonography (USG), computed tomography (CT) or MRI. We reviewed all available imaging studies evaluated by radiologist and classified each haemorrhage according to location (frontal lobe, parietal lobe, temporal lobe, occipital lobe and posterior fossa) and compartment (subarachnoid

 DOI:10.1097/MBC.0000000000000403
Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (www.bloodcoagulation.com).

haemorrhage, subdural, epidural, intraventricular and intraparenchymal haemorrhage) for each newborn. Medical follow-up records were obtained from the hospital files and prospective telephone interviews and/or clinical visits were also conducted.

The type of haemorrhage and overall haemorrhage severity were evaluated for all neonates. The haemorrhage type was determined according to the main type of haemorrhage, including subarachnoid, epidural, subdural, intraventricular and intraparenchymal haemorrhages. Subarachnoid haemorrhage was defined as haemorrhage beneath the subarachnoid space; epidural haemorrhage, haemorrhage between the dura and inner table of the cranium; subdural haemorrhage, haemorrhage between the brain and dura; intraventricular haemorrhage (IVH), haemorrhage in the lateral, third or fourth ventricles; and intraparenchymal haemorrhage, haemorrhage within the brain substance [3].

The severity of each neonate's haemorrhage was classified as mild, moderate or severe. Mild haemorrhage was defined as haemorrhage involving only one lobe and one compartment, with minimal or no mass effect or IVH in only one ventricle, with no hydrocephalus. Moderate haemorrhage was defined as haemorrhage involving only one lobe and one compartment, with mass effect or IVH in more than one ventricle, but no hydrocephalus. Severe haemorrhage was defined as haemorrhage involving more than one lobe or more than one compartment or IVH with hydrocephalus [3].

Haematological parameters including complete blood count (CBC), peripheral blood smear, activated partial thromboplastin time (aPTT), international normalized ratio (INR), fibrinogen, D-dimer, thrombin time (TT), protein C and protein S levels, factor XIII levels were noted from the hospital files if available and also measured prospectively in infants who could be evaluated in the follow-up visit. If aPTT and/or INR levels were increased beyond the normal range for their age, other factor levels (factor II, V, VII, VIII, IX, X, XI, XII) were also studied. If family history of the newborn revealed bleeding disorders, detailed haematological investigation was performed.

Postnatal follow-up examinations of these newborns have been performed by the neonatal follow-up clinic, paediatric haematology unit and/or paediatric neurology unit with the interval adjusted according to the patients' clinical status. Final status of each newborn was evaluated with telephone interviews and/or clinical visits. Each newborn was evaluated according to the physical and cognitive disability scale. Physical and cognitive disability scale was categorized as no disability, minor disability or major disability. Definitions of 'no disability', 'minor disability' or 'major disability' are shown in appendix, http://links.lww.com/BCF/A21 according to the scale developed by Jhawar *et al.* [3]. Informed consent was received by one of the parents for all neonates and the study protocol was approved by the local ethics committee of our hospital.

Results

During the study period of January 1994–January 2014, 16 term neonates were identified as having ICH in the Neonatal Intensive Care Unit of Hacettepe University Ihsan Dogramaci Children's Hospital, Ankara, Turkey. In six (37.5%) neonates, ICH was diagnosed during foetal life by obstetric ultrasonography and in 10 (62.5%) neonates, it was diagnosed after birth.

The mean gestational age was 38.2 ± 0.9 (37–40) weeks and mean birth weight was 3075 ± 660 g (2190–4320). Of these 16 term neonates with ICH, 12 (75.0%) were born by caesarean-section and four (25.0%) were born by vaginal delivery. Forceps was used for only one neonate (case no. 11). Four neonates were assessed as small for gestational age (SGA). The mean head circumference was 35.3 ± 2.7 (31–39) cm. Two newborns (12.5%) needed neonatal resuscitation at birth (case no 7 and 11). The mean Apgar score at first minute and at fifth minute was 7.0 ± 1.4 and 8.1 ± 1.2, respectively. The Apgar score of three newborns at 1 min was less than 7 (case nos. 7, 11 and 14) and Apgar score of two babies at 5 min was less than 7 (case nos. 7 and 11) (Table 1).

Intracranial haemorrhage was diagnosed during foetal life in six (37.5%) neonates and their mean gestational age was 33.5 ± 2.5 (31–36) weeks at the time of diagnosis. In 10 (62.5%) neonates, ICH was diagnosed after birth and their mean postnatal age was 1.9 ± 1.1 (1–4) days at the time of diagnosis. After birth, the diagnosis of ICH was confirmed by cranial USG in nine neonates, by cranial CT in seven neonates and by cranial MRI in nine neonates (more than one radiological imaging can be used in any newborn). Two neonates had USG, CT and MRI; four neonates had USG and MR; and two neonates had USG and CT for confirmation of the diagnosis and/or follow-up.

The haemorrhage type was IVH in eight (50.0%) neonates, intraparenchymal haemorrhage in six (37.5%) neonates, subarachnoid haemorrhage in one (6.25%) neonate and subdural haemorrhage in one (6.25%) neonate. The only case with multiple haemorrhages was case no. 15. In case no. 15, the site of haemorrhage was described as 'Giant haematoma at frontal lobe, diffuse intraventricular and subarachnoid haemorrhage'. As giant haematoma at frontal lobe occupied a wide place, the main haemorrhage type was defined as 'Intraparenchymal haemorrhage' for this case (Tables 1 and 2).

The most common ($n = 5/6$, 83.3%) haemorrhage type was IVH among neonates diagnosed during foetal life. IVH was identified in 30.0% ($n = 3/10$) of neonates who were diagnosed after birth. Overall haemorrhage severity was determined as mild in three (18.7%) neonates,

Table 1 Demographic and clinical characteristics of term neonates with foetal and neonatal intracranial haemorrhage

Parameters	Diagnosed during foetal life $n=6$	Diagnosed after birth $n=10$	Total $n=16$
Sex (male/female), *n*	2/4	6/4	8/8
Gestational age (weeks), mean ± SD (range)	38.1 ± 0.5 (37–38)	38.2 ± 1.2 (37–40)	38.2 ± 0.9 (37–40)
Mode of delivery (CS/vaginal), *n*	5/1	7/3	12/4
Birth weight (g), mean ± SD (range)	3384 ± 343 (2950–3800)	2904 ± 746 (2190–4320)	3075 ± 660 (2190–4320)
Resuscitation at birth, *n* (%)		2 (20.0)	2
Age at diagnosis of ICH (day), mean ± SD (range)	33.5 ± 2.5 (31–36)	1.9 ± 1.1(1–4)	
The haemorrhage type, *n* (%)			
Intraventricular	5	3	8 (50.0%)
Intraparenchymal	1	5	6 (37.5%)
Subarachnoid	–	1	1(6.3%)
Subdural	–	1	1 (6.3%)
Overall haemorrhage severity, *n* (%)			
Mild	–	3	3 (18.8%)
Moderate	1	2	3 (18.8%)
Severe	5	5	10 (62.5%)
Platelet count at birth (/μl) (mean ± SD (range)	289 000 ± 10 800 (128 000–443 000)	202 000 ± 10 500 (70 000–390 000)	229 000 ± 11 500 (70 000–443 000)
Thrombocytopenia at birth, *n* (%)	1	4	5 (31.25%)
Outcome, *n* (%)			
Died	1	3	4 (25.0%)
Survived	5	6	11 (68.8%)
Lost to follow-up	–	1	1 (6.3%)
Alive with disability, *n* (%) physical/cognitive disability scale	5	6	11
No disability	2	2	4 (36.4%)
Minor disability	–	1	1 (9.1%)
Major disability	3	3	6 (54.5%)

moderate in three (18.75%) neonates and severe in 10 (62.5%) neonates (Tables 1 and 2).

Haematological studies revealed that mean platelet count was 229 000 ± 11 500/μl (70 000–443 000/μl) at birth. Five (31.25%) neonates had thrombocytopenia (platelet count ≤150 000/μl) (case nos. 4, 9, 10, 11 and 14), while others had normal platelet count at birth. The causes of thrombocytopenia were early neonatal sepsis for case nos. 4, 9 and 10; perinatal hypoxia for case no. 11; and meconium aspiration syndrome for case no. 14.

One neonate had afibrinogenemia (fibrinogen level was 0 mg/dl) (case no. 15). He was the first child of his parents and there was no family history of a coagulation disorder. Cranial MRI revealed that he had a giant haematoma at frontal lobe with diffuse intraventricular and subarachnoid haemorrhages. He required mechanical ventilation during neonatal ICU follow-up period and he died at 21st day of his life.

The mean aPTT level was 40.7 ± 11.1 s (25.2–72.5) and mean INR level was 1.8 ± 1.7 (0.93–7.4) for the neonates with ICH. The mean fibrinogen level was 237.4 ± 130.3 mg/dl (0–460) and thrombin time was 18.2 ± 1.2 s (16.6–20.0). The mean protein C activity was 36.8 ± 23.3% (14–72%) and protein S activity was 53.4 ± 30.3% (10–99%). The mean ATIII level was 82.5 ± 39.2% (37–128%). The mean factor II level was 72.5 ± 21.5% (46–95%); factor V, 80.5 ± 23.3% (64–97%); factor VII, 110.0 ± 27.1% (54–125%); factor VIII, 132.1 ± 33.9% (99–191%); factor IX, 70.0 ± 19.7% (51–88%); factor X, 64.3 ± 18.0% (47–83%); and factor XIII, 93.7 ± 17.6% (90–100%). aPTT and INR levels were high in six neonates. Protein C, S, ATIII, factor II, V, VII, VIII, IX, X and XIII levels were normal for all neonates included in the study. The normal ranges of haematological parameters for term neonates were listed in Appendix 2, http://links.lww.com/BCF/A21.

Regarding therapy of neonates with ICH, in addition to routine vitamin K administration, the patients received fresh frozen plasma transfusions if the aPTT and INR were increased for their age. Fresh frozen plasma transfusion was required for six neonates; erythrocyte transfusion, for three neonates; and thrombocyte transfusion, for one neonate. Vitamin K administration was repeated in three neonates.

After discharge from the neonatal ICU, the mean duration of follow-up for these 16 term neonates with ICH was 42.8 ± 39.4 months (0.25–108 months). During follow-up, one infant was diagnosed with infantile spasm, one with cystic fibrosis, one with orofaciodigital syndrome and one with Friedrich ataxia. During the follow-up period, four (25.0%) neonates died, one (6.25%) neonate was lost to follow-up and 11 (68.75%) neonates survived. These infants are still being followed up in our hospital. During the follow-up period, three neonates underwent ventriculo-peritoneal (V-P) shunt operation for treatment of hydrocephalus. All three children who underwent V-P shunt operation survived.

The evaluation of physical and cognitive disability scales of the surviving children revealed that four (36.36%) had no disability, one (9.09%) had minor disability and six (54.5%) had major disability. The four children without disability have been attending their schools regularly.

Table 2 Site of haemorrhage, clinical and haematological risk factors, most severe haemorrhage type and overall haemorrhage severity in term newborn infants with intracranial haemorrhage

Case	Sex	Mode of delivery	Age at the time of diagnoses	Site of ICH	The haemorrhage type	Overall haemorrhage severity	Clinical and haematological risk factors	Treatment	Outcome
1	F	C/S	32nd week of gestation	Intraventricular haemorrhage in the left lateral ventricle	Intraventricular haemorrhage	Severe	She was diagnosed as infantile spasm (WEST syndrome) during infancy period	Left functional hemispherectomy	Alive with major physical and cognitive disability
2	M	C/S	32nd week of gestation	Triventricular hydrocephalus and intraventricular haemorrhage in the right lateral ventricle were noted on prenatal and postnatal ultrasonography	Intraventricular haemorrhage	Severe	–	–	Alive with no disability
3	F	C/S	36th week of gestation	Corpus callosum and cerebellar vermis hypoplasia; suprasellar hamartoma; dysplastic left cerebral hemisphere; cortical migration abnormality of right cerebral hemisphere and intraparenchymal haemorrhage in bilateral parieto-occipital lobes	Intraparenchymal haemorrhage	Severe	She was diagnosed as 'Orofaciodigital syndrome' She had macrocephaly, mass on the tongue and syndactyly	–	Alive with major physical and cognitive disability
4	M	C/S	31st week of gestation	Intraventricular haemorrhage in the bilateral lateral ventricles	Intraventricular haemorrhage	Severe	Platelet count: 128 000/μl	Spinal tap by neurosurgery V-P shunt operation Fresh frozen plasma	Alive with no disability
5	F	VD	36th week of gestation	Intraventricular haemorrhage at the posterior horn of right lateral ventricle	Intraventricular haemorrhage	Moderate	–	–	Expired at 2 years with pneumonia
6	M	C/S	34th week of gestation	Intraventricular haemorrhage in the right lateral ventricle	Intraventricular haemorrhage	Severe	–	–	Alive with major physical and cognitive disability
7	F	C/S	3rd day	Intraventricular haemorrhage in the right lateral ventricle	Intraventricular haemorrhage	Severe	–	Fresh frozen plasma and dexamethasone for brain oedema	Alive with major physical and cognitive disability
8	F	C/S	3rd day	Haemorrhage at putamen	Intraparenchymal haemorrhage	Mild	Congenital abnormalities including micrognathia, retrognathia, difficulty in swallowing	Erythrocyte transfusion	Expired at 5th month with aspiration pneumonia
9	M	V	2nd day	Intraventricular haemorrhage in the left third ventricle and bilateral lateral ventricles	Intraventricular haemorrhage	Moderate	Thrombocytopenia Platelet count: 70 000/μl	V-P shunt operation	Alive with minor physical and cognitive disability
10	F	C/S	1st day	Subarachnoid haemorrhage in bilateral parieto-occipital lobes	Subarachnoid haemorrhage	Moderate	Thrombocytopenia Platelet count: 117 000/μl	Fresh frozen plasma	Alive with no disability
11	M	V	1st day	Intraparenchymal haemorrhage in frontal lobe	Intraparenchymal haemorrhage	Severe	Thrombocytopenia Platelet count: 88 000/μl Resuscitation at birth Forceps delivery	Mechanical ventilation Fresh frozen plasma and platelet transfusion	Expired at 16th day of life
12	M	V	2nd day	Intraventricular haemorrhage at the anterior horn of right lateral ventricle	Intraventricular haemorrhage	Mild	–	Erythrocyte transfusion	Alive with no disability

Table 2 (*continued*)

Case	Sex	Mode of delivery	Age at the time of diagnoses	Site of ICH	The haemorrhage type	Overall haemorrhage severity	Clinical and haematological risk factors	Treatment	Outcome
13	F	V	4th day	Intraparenchymal haemorrhage at the left medial side of thalamus	Intraparenchymal haemorrhage	Mild	She was diagnosed as cystic fibrosis	–	Lost to follow-up
14	M	C/S	1st day	Intraparenchymal haemorrhage in bilateral parieto-occipital lobes and left temporal lobe	Intraparenchymal haemorrhage	Severe	Meconium aspiration syndrome Thrombocytopenia Platelet count: 125 000/μl He was diagnosed as 'Friedrich ataxia'	Fresh frozen plasma	Alive with major physical and cognitive disability
15	M	C/S	1st day	Giant haematoma at frontal lobe, diffuse intraventricular and subarachnoid haemorrhage	Intraparenchymal, intraventricular and subarachnoid haemorrhage	Severe	He was diagnosed as afibrinogenemia after birth Fibrinogen level was 0	Cryoprecipitate and fresh frozen plasma	Expired at 21st day of his life
16	F	C/S	1st day	Subdural haemorrhage at right hemisphere	Subdural haemorrhage	Severe	–	V-P shunt operation Erythrocyte transfusion	Alive with major physical and cognitive disability

C/S, caesarean/section; F, female; ICH, intracranial haemorrhage; M, male; V, vaginal delivery; V-P shunt, ventriculoperitoneal shunt.

Discussion

Although symptomatic ICH is a very rare event in term neonates, it has the potential to cause death or lifelong disability. Therefore, early diagnosis and treatment of ICH is very important in term neonates [9–11]. In a study performed by Sachs *et al.* [9], they reported that the incidence of ICH in term neonates was 12 among 23 000 deliveries (5.9/10 000 live births). In other studies, the incidences of ICH in term neonates were reported between 1.6 and 4.9/10 000 live births [10,11]. In our hospital, the incidence of ICH was 16 out of 11 389 (14/10 000) among term neonates. It is higher than the reported incidences. This may be due to the fact that our hospital is a university hospital (tertiary care centre) in Ankara, the capital city of Turkey. A lot of high-risk pregnant women and neonates are referred to the perinatology or neonatal ICUs of our hospital. In this case series, four neonates were transferred from other hospitals to our hospital.

Second stage of labour lasting more than 2 h, the use of oxytocin and deliveries with mechanical assistance such as forceps and vacuum-extraction were defined as obstetrical risk factors for development of ICH in term neonates [9]. In our study, forceps were used for one neonate and another neonate was intubated at birth for severe meconium stained amniotic fluid and meconium aspiration syndrome. Five neonates had low Apgar scores at first and fifth minutes indicating they suffered some degree of perinatal asphyxia. In our study, perinatal asphyxia secondary to meconium aspiration, low Apgar scores, resuscitation at birth and forceps application during delivery might have contributed to the development of ICH. The identifiable concurrent diseases included afibrinogenemia, infantile spasm, cystic fibrosis, orofaciodigital syndrome and Friedrich ataxia. Of these, only afibrinogenemia and cystic fibrosis have a reported association with ICH in the literature. These diseases might have facilitated the development of ICH in the term neonates in our study. In a study performed by Jhawar *et al.* [3], they determined that the requirement for resuscitation during birth, forceps assistance and lower Apgar scores at either first or fifth minute were each significant and independent predictors of ICH among full-term infants. In addition, they concluded that platelet count of 50 000/μl or less was associated with intraparenchymal haemorrhage and a more severe radiological grade of ICH [3]. In our case series, five (31.2%) neonates had thrombocytopenia (platelet count $\leq$150 000/μl) and two of them had intraparenchymal haemorrhage. However, their thrombocytopenia was mild (70 000, 88 000, 117 000, 125 000 and 128 000/μl) and only one neonate needed thrombocyte transfusion during the first month of his life.

In our case series, a total of seven (43.8%) neonates were identified as having thrombocytopenia, high aPTT and INR levels, and/or afibrinogenemia. So, the incidence of haematological disorders as a potential cause of bleeding

in term newborns was lower than our expectation. Therefore, ICH in term newborn infants seems to be caused primarily by other perinatal or neonatal factors not identified by our study.

In a previous study, most of the neonates reportedly became symptomatic by the second day of life [9]. In our study, ICH was diagnosed during foetal life in six (37.5%) term neonates at a median 32 weeks of gestation, whereas ICH was diagnosed in the other 10 (62.5%) neonates at a median of 2 days after birth.

In term neonates, different types of ICH may be observed. In a case series reported by Jhawar *et al.* [4], among 66 term neonates with ICH, intraparenchymal haemorrhage was observed in 21 (31.8%) term neonates; IVH in 20 (30.3%) neonates; subarachnoid haemorrhage in 14 (21.2%) neonates; and subdural haemorrhage in 11 (16.7%) neonates [4]. Intraventricular and intraparenchymal haemorrhage were the most common types of ICH among term neonates, whereas subarachnoid and subdural haemorrhages were less observed than the other types. In our case series, IVH was seen in eight (50%) neonates; intraparenchymal haemorrhage in six (37.5%) neonates; subarachnoid haemorrhage in one (6.25%) neonate; and subdural haemorrhage in one (6.25%) neonate. Neonates with IVH were mostly diagnosed (5/8) during foetal life. IVH might be easier to diagnose by ultrasonography during foetal life, especially at third trimester, whereas it is difficult to make differential diagnosis of intraparenchymal haemorrhage with ultrasonography [12].

Mental retardation, seizures, cerebral palsy and lower intelligence quotient levels are the most frequently reported disabilities in neonatal ICH. Follow-up should be extended to childhood and adolescence for these cases. In a study performed by Jhawar *et al.* [3], physical and cognitive disability scales were used for evaluation of children with ICH. In our case series, during median follow-up duration of 40.5 months, four (25.0%) neonates were expired; one (6.25%) neonate was lost to follow-up and 11(68.75%) neonates were alive. These 11 neonates have continued to be followed up in our hospital. If we considered physical and cognitive disability scales for these 11 children, four (36.36%) children had no disability, one (9.09%) child had minor disability and six (54.5%) children had major disability. Among four children who are alive with no disability, three had intraventricular and one had subarachnoid haemorrhage. On the contrary, among four neonates who had expired, three of them had intraparenchymal haemorrhage. Intraparenchymal haemorrhage might be more serious than other types of haemorrhages.

The presence of hydrocephalus requires early diagnosis, close monitoring and prompt surgical treatment. Early treatment may be an important factor for the neurodevelopmental outcome for the infants with ICH. In our case series, three neonates underwent V-P shunt operation for treatment of hydrocephalus. All three children who underwent V-P shunt operation are alive. One is alive with no physical and cognitive disability, one is alive with minor disability and the other is alive with major disability.

In conclusion, different types of haemorrhage including intraventricular, intraparenchymal, subarachnoid and subdural haemorrhage may occur in term neonates. Intraparenchymal haemorrhage might be more serious than other types of haemorrhages. In term neonates, in our series, haematological diseases and bleeding diseases did not appear to be the primary cause of ICH in most of our patients. Thus, detailed haematological investigation, search for other underlying diseases and follow-up are very important to find out the reason of ICH in term neonates. Furthermore, early diagnosis, close monitoring and prompt surgical interventions are important factors to reduce disabilities. During foetal life, especially at third trimester, ultrasonography enables us to perform early diagnosis and therapeutic interventions.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

References

1 Lo WD, Lee J, Rusin J, Perkins E, Roach ES. Intracranial hemorrhage in children: an evolving spectrum. *Arch Neurol* 2008; **65**:1629–1633.
2 Chamilos C, Sgouros S. Intrauterine grade IV intraventricular hemorrhage in a full-term infant leading to hydrocephalus. *Childs Nerv Syst* 2013; **29**:861–865.
3 Jhawar BS, Ranger A, Steven DA, Del Maestro RF. A follow-up study of infants with intracranial hemorrhage at full-term. *Can J Neurol Sci* 2005; **32**:332–339.
4 Jhawar BS, Ranger A, Steven D, Del Maestro RF. Risk factors for intracranial hemorrhage among full-term infants: a case–control study. *Neurosurgery* 2003; **52**:581–590.
5 Brouwer AJ, Groenendaal F, Koopman C, Nievelstein RJ, Han SK, de Vries LS. Intracranial hemorrhage in full-term newborns: a hospital-based cohort study. *Neuroradiology* 2010; **52**:567–576.
6 Fenichel GM, Webster DL, Wong WK. Intracranial hemorrhage in the term newborn. *Arch Neurol* 1984; **41**:30–34.
7 Sandberg DI, Lamberti-Pasculli M, Drake JM, Humphreys RP, Rutka JT. Spontaneous intraparenchymal hemorrhage in full-term neonates. *Neurosurgery* 2001; **48**:1042–1048.
8 Bergman I, Bauer RE, Barmada MA, Latchaw RE, Taylor HG, David R, *et al.* Intracerebral hemorrhage in the full-term neonatal infant. *Pediatrics* 1985; **75**:488–496.
9 Sachs BP, Acker D, Tuomala R, Brown E. The incidence of symptomatic intracranial hemorrhage in term appropriate-for-gestation-age infants. *Clin Pediatr (Phila)* 1987; **27**:355–358.
10 Hanigan WC, Powell FC, Miller TC, Wright RM. Symptomatic intracranial hemorrhage in full-term infants. *Childs Nerv Syst* 1995; **11**:698–707.
11 Hojberg AS, Ebbesen F, Lund EB, Agerholm H. Neurodevelopmental outcome in fullterm infants with symptomatic intracranial haemorrhage of unknown aetiology. *Dan Med Bull* 1997; **44**:439–442.
12 Ghi T, Simonazzi G, Perolo A, Savelli L, Sandri F, Bernardi B, *et al.* Outcome of antenatally diagnosed intracranial hemorrhage: case series and review of the literature. *Ultrasound Obstet Gynecol* 2003; **22**:121–130.
13 Brugnara C. Reference values in infancy and childhood. In Orkin SH, Nathan DG (editors). *Nathan and Oski's hematology of infancy and childhood.* 7th ed. Saunders/Elsevier; 2009. pp. 1784–1790 (cited in Appendix 2).