

Al-Azhar International Medical Journal

Volume 4 | Issue 6

Article 33

2023 Section: Pediatrics & its Subspecialty.

Neonatal and Obstetric Risk Factors of Intracranial Haemorrhage in Preterm Infants

Hassan Ali Hassan Department of Pediatrics, Faculty of Medicine for boys, Al-Azhar University, Cairo, Egypt.

Ahmed Mohamed Ismail Department of Pediatrics, Faculty of Medicine for boys, Al-Azhar University, Cairo, Egypt.

Maged Mohamed Ali Ataki Department of Radiology, Faculty of Medicine for boys, Al-Azhar University, Cairo, Egypt.

Ahmed AbdelKhalek Deshnawy Department of Pediatrics, Faculty of Medicine for boys, Al-Azhar University, Cairo, Egypt., moazelmanzlawy33@gmail.com

Follow this and additional works at: https://aimj.researchcommons.org/journal

Part of the Medical Sciences Commons, Obstetrics and Gynecology Commons, and the Surgery Commons

How to Cite This Article

Hassan, Hassan Ali; Ismail, Ahmed Mohamed; Ataki, Maged Mohamed Ali; and Deshnawy, Ahmed AbdelKhalek (2023) "Neonatal and Obstetric Risk Factors of Intracranial Haemorrhage in Preterm Infants," *Al-Azhar International Medical Journal*: Vol. 4: Iss. 6, Article 33. DOI: https://doi.org/10.58675/2682-339X.1842

This Original Article is brought to you for free and open access by Al-Azhar International Medical Journal. It has been accepted for inclusion in Al-Azhar International Medical Journal by an authorized editor of Al-Azhar International Medical Journal. For more information, please contact dryasserhelmy@gmail.com.

ORIGINAL ARTICLE

Neonatal and Obstetric Risk Factors of Intracranial Haemorrhage in Preterm Infants

Hassan Ali Hassan ^a, Ahmed Mohamed Ismael ^a, Maged Mohamed Ali Ataki ^b, Ahmed AbdelKhalek Deshnawy ^a,*

^a Department of Pediatrics, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt

^b Department of Radiology, Faculty of Medicine for Boys, Al-Azhar University, Cairo, Egypt

Abstract

Background: Intracranial haemorrhage (ICH) in the preterm baby is an acquired lesion with a large potential impact on morbidity, mortality, and long-term neurodevelopmental prognosis.

Objective: The goal of this study was to detect the incidence of intracranial haemorrhage in preterm and its relationship to obstetric and neonatal risk factors.

Methods: 100 preterm infants will be a part of this upcoming cross-sectional study. The Neonatal Intensive Care Unit (NICU) for Children at Al-Azhar University Hospitals served as the study's location (Al Hussein and Sayed Galal), the patients underwent cranial ultrasonography after being chosen on a non-randomized, selective sampling basis in accordance with the inclusion criteria.

Results: There is a sizable difference between the groups in terms of GA and birth weight, however, there is no discernible difference in terms of foetal discomfort, asphyxia resuscitation, and elevated neonatal CRP.

Conclusion: Failure to administer prenatal steroids is connected with intracranial bleeding in premature infants, histological chorioamnionitis, lower amniotic fluid index and elevated maternal leukocyte count, GA, birth weight, Apgar at 1 min & asphyxia resuscitation. To lower the incidence and severity of neonatal ICH, for instance, coverage of (full) prenatal steroid medication should be improved. Clinicians and healthcare policymakers should take these aspects into consideration when making decisions. Additional research in a larger cohort of newborns with Middle Eastern descent is necessary to assess all potential risk factors that may be specific to this community.

Keywords: Infants, Intracranial haemorrhage, Neonatal, Obstetric, Preterm, Risk factors

1. Introduction

B irth trauma causes 1–2% of newborn deaths, and severe cerebral damage manifest in the first few days after birth as irritability, poor feeding, emesis, apnea, disordered breathing, bradycardia, seizures, or mentation problems.¹

An acquired brain injury that has a significant potential to affect morbidity, mortality, and longterm neurodevelopmental outcomes is intracranial haemorrhage (ICH) in preterm infants. Despite much enhanced newborn care and a rise in preterm baby survival over the past few decades, ICH is still a grave concern.² The likelihood of symptomatic ICH in full-term neonates has been linked to a number of factors, including mother parity, foetal weight, aided vaginal delivery (with forceps or vacuum extraction), and protracted labour.³

New advancements in neonatal imaging, brain monitoring, hemodynamics, and a deeper comprehension of inflammatory and genetic pathways have all contributed to the ongoing progress in our understanding of ICH in premature infants, which present new difficulties for the development of early detection and prevention methods.⁴

Although the frequency and distribution of ICH in preterm neonates are unclear, imaging studies show

Accepted 26 December 2022. Available online 30 December 2023

https://doi.org/10.58675/2682-339X.1842 2682-339X/© 2023 The author. Published by Al-Azhar University, Faculty of Medicine. This is an open access article under the CC BY-SA 4.0 license (https://creativecommons.org/licenses/by-sa/4.0/).

^{*} Corresponding author at: Department of Pediatrics, Faculty of Medicine for boys, Al-Azhar University, Cairo, 11618, Egypt. Fax: 20225065579. E-mail address: moazelmanzlawy33@gmail.com (A. AbdelKhalek Deshnawy).

that it can happen to babies. The prevalence of IC haemorrhage in infants was found to be 37.8% according to the findings of one sizable prospective study including imaging by Nikam et al.⁵; the majority of haemorrhages were linked to vaginal birth.

In addition, subdural bleeding, which can occur in up to 90% of cases in young infants with abusive head trauma (AHT), is the most often reported intracranial pathology.¹

The goal of this study was to detect the incidence of intracranial haemorrhage in preterm and its relationship to obstetric and neonatal risk factors.

2. Patients and methods

There will be 100 premature babies included in this prospective cross-section investigation. The study was carried out at the Al-Azhar University Hospitals' Neonatal Intensive Care Unit (NICU) for Children (Al Hussein and Sayed Galal), The patients were chosen using nonrandomized purposive sampling methods in accordance with the inclusion criteria, and cranial ultrasonography was performed on them. The sample size for this study was determined using 5 Epi Info STATCALC, which was based on the study conducted by Nikam et al., taking into account the following hypotheses: A power of 80% and a two-sided confidence level of 95%. & estimated odds ratio = 1.115 with a 5% error. From the Epi-Info output, a maximum sample size of 146 was ultimately used. The sample size was therefore raised to 150 cases in order to account for potential drop-off in cases during follow-up.

2.1. Inclusion criteria

Preterm neonates <36 weeks gestational age admitted to the NICU of Pediatric Department of Al-Azhar University Hospitals (Al Hussein and Sayed Galal).

2.2. Exclusion criteria

Significant congenital defects seen on ultrasound at 18–20 weeks of pregnancy, full-term newborns >37 weeks, and major maternal illnesses both hydrocephalus and.

2.3. Methods

All patients were suspected to:

The following obstetric information will be gathered: the mother's age, ethnicity, whether she gave birth naturally or under anaesthesia, whether she used forceps or a vacuum to help her deliver naturally, and the length of her labour. length of a membrane rupture as well as maternal trauma. We will gather information on the following neonatal issues: the occurrence of neonatal infection, neonatal asphyxia, neonatal apnea, neonatal seizures, and length of hospital stay. , birth weight, gestational age at birth, and neonatal head circumference comprehensive medical examination Vital indicators (temperature, heartbeat, respiration, blood pressure), symptoms of (Pallor, Cyanosis, and Jaundice).

Finding the Apgar score at 1 and 5 min postpartum: An Apgar score consists of five components. Every category is equally weighted and given a value of 0, 1, or 2. At 1 and 5 min after delivery, a total score is calculated by adding the individual components. In full-term and late preterm newborns, a score of 0-3 is seen as low, a score of 4-6 is regarded as highly aberrant, and a score of 7-10 is regarded as reassuring. Neonatal Resuscitation Program guidelines advise continuing recording at 5-min intervals up to 20 min if an infant has a score of less than 7 at 5 min.

Every infant whose participation in the study was authorised had cranial ultrasonography. The size of the largest SDH among infants who had SDH in various places was noted. Cephalohematoma's existence will also be noted. When a newborn is born with bruising from the use of forceps, a cephalohematoma, a scalp laceration, or another outward sign of neonatal birth trauma, we will note this.

2.4. Ethical considerations

The protocol was submitted for the Research Ethics Committee's approval. All information was kept private. Every participant has the option to leave the study without it having an impact on their management.

2.5. Statistical analysis

SPSS Inc., Chicago, IL, USA, provided MedCalc 13 for Windows and SPSS 22.0 for Windows for the collection, tabulation, and statistical analysis of all data (MedCalc Software bvba, Ostend, Belgium). Each statistical comparison was subjected to the two-tailed significance test. *P* values of 0.05 and 0.001 indicate highly significant differences, respectively, whereas P > 0.05 indicates no difference at all.

3. Results

Table 1.

Table 1. Intracranial haemorrhage incidence among preterm neonates.

	Studied patients ($N = 150$)
ICH	31 (20.7%)
None	119 (79.3%)

This table shows that incidence of ICH was 20.7% Table 2.

There is a significant difference between the two studied groups regarding BMI Tables 3 and 4.

This table shows that there is no significant difference between the groups Table 5.

This table shows that there is a significant difference between the groups regarding GA and birth weight Table 6.

4. Discussion

The World Health Organization defines a preterm birth as any birth that takes place before 37 full weeks of pregnancy (or 259 days after the mother's last menstrual period), whichever occurs first. Low birth weight (LBW; 1500–2500 g), very low birth weight (VLBW; 1000–1499 g), and extremely low birth weight are further classifications for preterm births (ELBW; 1000 g). The most severe side effect of premature birth, intraventricular haemorrhage (IVH), is especially damaging to newborns with birth weights under 1500 g and gestational ages under 32 weeks since it results in both short- and long-term morbidities.⁶

Prolonged labour, improper masculine behaviour, membrane rupture before the lining of the uterus, as well as uterine infection Respiratory distress syndrome, metabolic acidosis, postnatal resuscitation, and an early onset of newborn infection are a few recognised risk factors for cerebral haemorrhage in premature infants.⁷

The patients' average BMI was 27.61 kg/m2, and their average age was 28.73 years. 40% of patients were primigravida, while 60% of patients were multiparous. Age, BMI, and parity between the two study groups (ICH n = 31 & normal n = 69) were not substantially different. 31% of ICH cases were reported.

Table 2. Demographic data distribution according to presence of ICH.

	ICH (N = 31)	Normal (<i>N</i> = 119)	t	Р
Age (years) Mean ± SD	27.39 ± 4.51	28.19 ± 4.93	0.818	0.415
BMI (kg/m ²)				
Mean \pm SD	26.28 ± 2.67	27.34 ± 2.48	2.1	0.039
Parity			χ^2	Р
Primigravida	11 (35.5%)	49 (41.2%)	0.332	0.564
Multiparous	20 (64.5%)	70 (58.8%)		

Table 3. Maternal risk factors distribution according to presence of ICH This table shows that there was no significant difference between the groups.

ICH (N = 31) N (%)	Normal (N = 119) N (%)	Р
GDM 2 (6.5)	10 (8.4)	0.721
Pre-eclampsia 10 (32.3)	36 (30.3)	0.829
Histological 19 (61.3) chorioamnionitis	58 (48.7)	0.213
Clinical 14 (45.2) chorioamnionitis	41 (34.5)	0.272
PROM 13 (41.9)	37 (31.1)	0.255
Abnormal CTG 16 (51.6)	57 (47.9)	0.713
Pneumothorax 12 (38.7)	32 (26.9)	0.198
Maternal infection 9 (29)	23 (19.3)	0.241

Table 4. Maternal history of medications distribution according to presence of ICH.

	ICH (N = 31) N (%)	Normal (N = 119) N (%)	Р
Steroids	17 (54.8)	55 (46.2)	0.392
Antibiotics	19 (61.2)	61 (51.3)	0.319
MgSO ₄	10 (32.3)	58 (48.7)	0.101
Ritodrine hydrochloride	21 (67.7)	66 (55.5)	0.218
Infertility drugs	10 (32.3)	22 (18.5)	0.096

Our results agreed with the study by Al-Mouqdad et al.,⁸

Due to the fact that they included 108 infants without IVH cases and 108 infants with IVH cases, the case group comprised 108 IVH cases. The demographics of the case and control groups did not differ significantly from one another. Similar to this, Lu et al., 9 discovered that maternal factors did not significantly differ between ICH patients and controls, compared to 29.8 6.1 years for controls, patients' mothers had a mean age of 28.6 6.2 years (P = 0.143). Both the number of pregnancies and the technique of birth were the same for the mothers of cases and controls (P = 0.438, P = 0.659).

Table 5. Neonatal characteristics distribution according to presence of ICH.

	ICH (N = 31)	Normal (<i>N</i> = 119)	Р
GA (weeks)			
Mean \pm SD	29.1 ± 2.83	32.65 ± 2.45	<0.001
Birth weight (kg)		
Mean \pm SD	972 ± 164	1285 ± 181	< 0.001
Apgar at 1 min			
Mean \pm SD	6.65 ± 1.95	7.22 ± 2.03	0.163
Apgar at 5 min			
Mean \pm SD	7.81 ± 2.16	8.25 ± 2.43	0.360
Gender			
Male	18 (58.1%)	65 (54.6%)	0.731
Female	13 (41.9%)	54 (45.4%)	

Table 6. Neonatal risk factors distribution according to presence of ICH.

	ICH (N = 31) N (%)	Normal (N = 119) N (%)	Р
Fetal distress	18 (58.1%)	41 (34.5%)	0.017
Asphyxia resuscitation	21 (67.7%)	45 (37.8%)	0.003
Elevated neonatal CRP	9 (29%)	9 (7.6%)	0.001
Early-onset sepsis	5 (16.1%)	9 (7.6%)	0.144
		<i>a</i> 11 <i>6</i> 1	

This table shows that there is no significant difference between the groups regarding fetal distress, asphyxia resuscitation, and elevated neonatal CRP.

The present study showed that as regard Maternal risk factors distribution among the studied patients; the most common risk factor was histological chorioamnionitis (51%) followed by abnormal CTG (48%). There was a significant difference between the groups (ICH n = 31 & normal n = 69) regarding histological chorioamnionitis. Our findings were validated by the research by Lu et al.,⁹ They found that the likelihood of IVH was positively connected with the diagnosis of histological chorioamnionitis, which was diagnosed more frequently in cases' pregnancies (63.6%) than in controls' (37.5%). However, Data suggesting each clinical chorioamnionitis symptom, such as higher maternal CRP, leukocyte count, or maternal temperature, showed no differences. Patients were detected with prolonged membrane rupture substantially more frequently than controls. When researchers looked at variations in IVH in relation to latency period in patients with preterm premature rupture of membranes (pPROM), they found no connection between the two. Factors including gestational diabetes and preeclampsia did not significantly differ between cases and controls. Numerous questions still need to be resolved regarding the connection between IVH and protracted delay following pPROM. However, extended latency increases chorioamnionitis or intrauterine foetal infection, They have both been recognised as potential early signs of brain injury in both human and animal models.¹⁰

The embryonic body produces proinflammatory cytokines such tumour necrosis factor and interleukin-6 as a result of intrauterine infections, according to Leviton's¹¹ theory, which eventually results in brain damage. Later, a few years, interleukin-6 concentrations in the umbilical cord plasma were found to significantly correlate with IVH, according to Yoon et al..¹² and Gomez et al..¹³ As a result, it stands to reason that the severity of IVH in preterm neonates may seem to worsen with longer delays. Also, in the study of Huang *et al.*,¹⁴ Odds ratios ([OR] 2.18, 95% confidence intervals [CI] 1.58-2.99), mild IVH ([OR] 1.95, 95% CI 1.09-3.49), and severe IVH ([OR] 2.65, 95% CI 1.52-4.61) were all enhanced by prenatal infection. The ORs and 95% CI for prenatal infection type were as follows: 2.21 (1.60-3.05), 2.26 (1.55-3.28), 1.88 (1.22-2.92), and 1.88 (1.14-3.10) for chorioamnionitis, histologic chorioamnionitis, and ureaplasma, respectively.

The current study showed that as regard Maternal history of medications distribution among the studied patients: the most common medication used was steroid (80%) followed antibiotics (85%). There is a significant difference between the groups regarding steroids, antibiotics, and MgSO4.

Our results were supported by a Cochrane review held by **Roberts & Dalziel**,¹⁵ consisted of a metaanalysis of randomized trials showed a lower incidence of IVH when prenatal steroids were used (relative risk = 0.54, 95% confidence interval: 0.43 to 0.69).

Our results were in line with those of Wei et al..¹⁶ who discovered that antenatal steroid use was linked to lower rates of severe intraventricular haemorrhage (odds ratio = 0.51, In 25 979 children with very low birth weight, the odds ratio for any grade of intraventricular haemorrhage is 0.68, with a 95% confidence interval of 0.62-0.75. Similarly, Özek & Kersin,¹⁷ demonstrated that it is observed less frequently germinal matrix-IVH in the female, black race, and with antenatal steroid use. Furthermore, Poryo et al.,¹⁸ revealed that using catecholamines was linked to a higher risk of IVH for all enrolled neonates, although prenatal steroids (ANS) before the onset of labour were shown to be linked to a lower risk of IVH overall. In the study in our hands, mean amniotic fluid index was 109.63 ± 20.54 mm. Moreover, higher maternal temperature was found in 20 women (20%), elevated maternal leukocyte count was found in 45 women (45%) and elevated maternal CRP was found in 24 women (24%). There is a significant difference between the groups regarding amniotic fluid index and elevated maternal leukocyte count. In accordance with our results study of Lu et al.,9 because they asserted that the case group's AFI was lower than the controls' AFI. A univariate analysis revealed a strong relationship between AFI and IVH. AFI is regarded as a significant indicator of healthy placental function. Lower AFI in third-trimester prenatal testing is associated with a higher risk of unfavourable perinatal outcomes, such as intrauterine growth restriction and intrapartum foetal distress, claim Gumus et al.¹⁹

According to a Locatelli et al.,²⁰ study, In low-risk pregnancies past 40 weeks, oligohydramnios increases the likelihood of a poor neonatal outcome.

According to the current study's findings, the average gestational age was 30.63 weeks, the average birth weight was 1019 206 g, and the average Apgar score at 1 min was 6 2, and the mean Apgar at 5 min was 8 2. Asphyxia resuscitation was the most frequent risk factor (43%) and was followed by foetal distress (59%). The groups differ significantly in terms of GA, birth weight, and Apgar at 1 min Asphyxia resuscitation differs significantly between the groups in a major way.

In accordance with our results study of Ertan *et al.*,²¹ as they shown that the main risk factors for the development of IVH are low birth weight and gestational age. According to Sankaran et al.,²² birth weight is the most significant prenatal and perinatal factor. Additionally, Vural et al.,²³ in Turkey observed occurrences of IVH in infants weighing 500–2000 g, ranging, respectively, from 37% to 5%. Before 35 weeks of pregnancy, IVH is more common.

Infants at a gestational age of 22-32 weeks were found to have periventricular leukomalacia and white matter abnormalities in Larroque et al.²⁴ 's study. The mean gestational age for the patients and controls in the Lu et al. research⁹ was 986 122 g and 1274 153 g, respectively. In cases, the mean gestational age was 29.3 2.8 weeks, whereas in controls, it was 32.7 2.5 weeks. Compared to neonates in the control group, babies in the case group were born with lower birth weights and gestations (P.001), according to a univariate analysis. More commonly than controls, cases required resuscitation of hypoxia and caused pain in the foetus. Significant correlations were found between low Apgar scores at 5 min and a higher IVH. There were no obvious differences in early-onset sepsis, neonatal CRP, or gender between IVH patients and controls. Similar to this, Bauer et al.²⁵ demonstrated that low birth weight and decreased gestational age are the primary causes of IVH in premature infants. According to certain studies, IVH and suffocation are related in premature newborns. Although the precise processes are unknown, resuscitation with high oxygen concentration following hypoxia might exacerbate IVH by boosting hyperoxemia and oxidative stress.²⁶

In addition, **Poryo** *et al.*,¹⁸ showed that in all enrolled babies, higher GA was related with a reduced risk of IVH and that higher RDS and pneumothoraces were associated with a higher risk of IVH. Between ICH cases and controls, the mean gestational age (P = 0.372) and mean baby weight (P = 0.919), however, were comparable, as would be predicted from matching, according to Al-Mouqdad et alstudy.

4.1. Conclusion

Failure to administer prenatal steroids is connected with intracranial bleeding in premature infants., histological chorioamnionitis, lower amniotic fluid index and elevated maternal leukocyte count, GA, birth weight, Apgar at 1 min & asphyxia resuscitation. To lower the incidence and severity of neonatal ICH, for instance, coverage of (full) prenatal steroid medication should be improved. Clinicians and healthcare policymakers should take these aspects into consideration when making decisions. Additional research in a larger cohort of newborns with Middle Eastern descent is necessary to assess all potential risk factors that may be specific to this community.

Disclosure

The authors have no financial interest to declare in relation to the content of this article.

Authorship

All authors have a substantial contribution to the article.

Sources of funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Conflict of interest

There are no conflicts of interest.

References

- Choudhary AK, Servaes S, Slovis TL, et al. Consensus statement on abusive head trauma in infants and young children. *Pediatr Radiol.* 2018;48:1048–1065.
- Donia AES, Hassan HA. Incidence of intraventricular hemorrhage in preterm neonates in NICU at Bab–Elsharyia university hospital. *AL-Azhar Med*, J. 2012;41:887–901.
- 3. Chung CC, Chan L, Bamodu OA, Hong CT, Chiu HW. Artificial neural network based prediction of postthrombolysis intracerebral hemorrhage and death. *Sci Rep.* 2020;10:1–10.
- Lignelli E, Palumbo F, Myti D, Morty RE. Recent advances in our understanding of the mechanisms of lung alveolarization and bronchopulmonary dysplasia. *Am J Physiol Lung Cell Mol Physiol.* 2019;317:L832–L887.
- Nikam RM, Kandula VV, Yue X, et al. Birth-related subdural hemorrhage: prevalence and imaging morphology. *Pediatr Radiol.* 2021;2:1–8.
- 6. Howes A, Hilditch C, Keir A. What clinical practice strategies have been shown to decrease incidence rates of intraventricular haemorrhage in preterm infants? *J Paediatr Child Health.* 2019;55:1269–1278.

- Egesa WI, Odoch S, Odong RJ, et al. Germinal matrix-intraventricular hemorrhage: a tale of preterm infants. *Int J Pediatr.* 2022;57:37S-45S.
- Al-Mouqdad MM, Abdelrahim A, Abdalgader AT, et al. Risk factors for intraventricular hemorrhage in premature infants in the central region of Saudi Arabia. *Int J Pediatr Adoles Med.* 2021;8:76–81.
- Lu H, Wang Q, Lu J, Zhang Q, Kumar P. Risk factors for intraventricular hemorrhage in preterm infants born at 34 weeks of gestation or less following preterm premature rupture of membranes. J Stroke Cerebrovasc Dis. 2016;25:807–812.
- Rocha G, Proenca E, Quintas C. Chorioamnionitis and brain damage in the preterm newborn. J Matern Fetal Neonatal Med. 2007;20:745–749.
- Leviton A. Preterm birth and cerebral palsy: is tumor necrosis factor the missing link? Dev Med Child Neurol. 1993;35:553–558.
- Yoon BH, Romero R, Yang SH. Interleukin-6 concentrations in umbilical cord plasma are elevated in neonates with white matter lesions associated with periventricular leukomalacia. *Am J Obstet Gynecol.* 1996;174:1433–1440.
- 13. Gomez R, Romero R, Ghezzi F. The fetal inflammatory response syndrome. *Am J Obstet Gynecol*. 1998;179:194–202.
- 14. Huang J, Meng J, Choonara I, et al. Antenatal infection and intraventricular hemorrhage in preterm infants: a metaanalysis. *Medicine*. 2019;98, e16665.
- 15. Roberts D, Dalziel S. Antenatal corticosteroids for accelerating fetal lung maturation for women at risk of preterm birth. *Cochrane Database Syst Rev.* 2006;3:CD004454.
- Wei JC, Catalano Ř, Profit J, Gould JB, Lee HC. Impact of antenatal steroids on intraventricular hemorrhage in verylow-birth weight infants. J Perinatol. 2016;36:352–356.

- 17. Özek E, Kersin SG. Intraventricular hemorrhage in preterm babies. *Turk Pediatri arsivi*. 2020;55:215-221.
- Poryo M, Boeckh JC, Gortner L, et al. Ante-, peri-and postnatal factors associated with intraventricular hemorrhage in very premature infants. *Early Hum Dev.* 2018;116:1–8.
- Gumus II, Koktener A, Turhan NO. Perinatal outcomes of pregnancies with borderline amniotic Xuid index. Arch Gynecol Obstet. 2007;276:17–19.
- Locatelli A, Zagarella A, Toso L. Serial assessment of amniotic fluid index in uncomplicated term pregnancies: prognostic value of amniotic fluid reduction. J Matern Fetal Neonatal Med. 2004;15:233–236.
- Ertan AK, Tanriverdi HA, Meier M, Schmidt W. Perinatal risk factors for neonatal intracerebral hemorrhage in preterm infants. Eur J Obstet Gynecol Reprod Biol. 2006;127:29–34.
- 22. Sankaran E, Kushnir Brandsma A. Effect of administration of normal saline bolus on intraventricular hemorrhage in preterm neonates. *Pediatrics*. 2018;141(1 MeetingAbstract):517.
- Vural M, Yilmaz I, Ilikkan B. Intraventricular hemorrhage in preterm newborns: risk factors and results from a University Hospital in Istanbul, 8 years after. *Pediatr Int.* 2007;49: 341–344.
- 24. Larroque B, Marret S, Ancel PY. White matter damage and intraventricular hemorrhage in very preterm infants: the EPIPAGE study. *J Pediatr*. 2003;143:477–483.
- Bauer M, Fast C, Haas J. Cystic periventricular leukomalacia in preterm infants: an analysis of obstetric risk factors. *Early Hum Dev.* 2009;85:163–169.
- Markus T, Hansson S, Amer-Wahlin I. Cerebral inflammatory response after fetal asphyxia and hyperoxic resuscitation in newborn sheep. *Pediatr Res.* 2007;62:71–77.