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Preterm screening by transfontanelar ultrasound – results of a 5 years cohort study

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Abstract

Objectives: Intracranial hemorrhages (ICH) might be the cause of significant psycho-motor or cognitive impairment in preterm babies. A 5 year cohort study performed in the IOMC was aimed at determining the prevalence and proportion of the main types of ICH diagnosed by transfontanelar (TF) ultrasound among admitted preterms, along with the neuro-developmental effects on a 12 month follow-up period. **Material and methods:** In the above mentioned period all enrolled newborns were examined by TF ultrasound according to a common standardized protocol. The 4 grade Papile ICH classification was used for all examined subjects. In order to determine the potential neurological sequels we performed a 12 month neurological follow-up of all 292 patients in the study group. **Results:** The prevalence of all types ICH diagnosed by systematic TF ultrasound was 20.4 %. The most prevalent type of ICH was peri-intraventricular: 40% grade I and 33 % grade II, with no major neurological sequels For both the correlation to the neurological outcome was statistically significant ($p < 0.05$). Severe neurological sequels were associated with grade III and IV, but the correlation was found to be statistically significant ($p<0,05$) only for grade IV hemorrhages. A severe neurological outcome was of statistical significance only for the cerebellar hemorrhage outcome, although a similar pattern was also observed for the thalamic hemorrhages. **Conclusion:** Systematic TF screenings for preterm is useful for early diagnosis and staging which might improve the management of rehabilitation therapies, and provide appropriate information on the disease outcome as well as influencing the quality of parental counseling.

Keywords: preterm, screening, transfontanelar ultrasound, neurological outcome.

Introduction

The importance of preterm screening by transfontanelar (TF) ultrasound is sustained by the observation that in this vulnerable group, babies who are found to have abnormal brain scans are usually asymptomatic. Only occasionally these patients develop symptoms (seizures or other neurological symptoms) due to a massive intracranial hemorrhage (ICH). In most countries, the routine screening in preterm was imposed by the high incidence of intracranial bleeding, first revealed by systematic computerized tomography studies in preterm babies [1,2].

Since the early 1980s, as ultrasound became widely available, an important number of cohort studies revealed a high incidence of all types of intracranial hemorrhages in preterm [3,4]. Although in the last years most studies demonstrate a decrease in the overall incidence, with a lower number of parenchymal lesions, the prevalence of disability in the survivors remains disproportionately high [5,6].

Till now, no systematic studies concerning a preterm TF ultrasound follow-up in Romania have been published. The aim of this study is to determine the preva-

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lence and the proportion of the main types of ICH diagnosed by TF ultrasound among preterm newborns admitted in the IOMC during a 5 year period. In order to determine the potential neurological sequels, known to be associated with some types of ICH, we performed a 12 month follow-up of all patients in the study group.

Material and methods

The study performed over a 5 year period (2006-2010) in the Ist Pediatric Clinic – Institute for Mother and Child Care (IOMC) "Prof. Dr. Alfred Rusescu" Bucharest, consisted of a prospective follow-up of a total number of 302 cases. In the above-mentioned period from the total number of 42,360 admitted children, 1480 were preterm babies, defined as children born at less than 37 weeks gestational age [7].

All preterms were evaluated by systematic transfontanelar ultrasound. An ICH diagnostic was established in 302 cases. A neuro-developemental follow-up of this selected subjects was performed during a 12 month period.

I Informed consent, along with the Ethical Committee approval were obtained for all enrolled subjects.

The ultrasound examination was performed according to a standardized protocol. Multiple coronal and sagital scans through the anterior and posterior fontanels were obtained at each examination. Color and pulsed wave Doppler interrogation was also performed systematically. Aloka SSD 5500 and General Electric Logiq 300 machines, both with appropriate probes for neonatal head examination (5-10 MHz frequency) were used. The TF examinations were completed by two specialists, trained for newborn and pediatric cranial ultrasound.

The newborns were ultrasonographically first examined at 3- 8 days postnatal age, then between 14-21 days postnatal age, monthly in the first 3 postnatal months, and every 3 months between 3-12 months. The ultrasound diagnostic criteria used in all cases were based on the Papile and Volpe classification [8,9]. A grade I hemorrhage is strictly confined to the germinal matrix, a grade II hemorrhage occupies less than 50% of one of the lateral ventricles, in the grade III hemorrhage the lateral ventricles are distended more than 50%. Grade IV, secondary to venous infarction consists of hemorrhage into both the ventricular system and cerebral parenchyma.

The neurological examination was performed in the same day with the ultrasound diagnosis and every 3 months till the first birthday. Examinations were performed by the same pediatric neurologist. In the neurological outcome the minimal neurological sequels were considered to be mild motor retardation and/or speech and language delay. The cerebral palsy, sensorial dysfunctions, mental retardation, motor retardation, and epilepsy were considered as major neurological sequels.

Data underwent a statistical analysis and results were compared to available data in the literature. The Chi-squared test was performed in order to demonstrate statistically significant differences between groups. Data are presented as number and percents.

Results

From a total number of 42,360 hopitalizations in the 5 year period, 1480 newborns were preterm (3.49% of all admitted children). The ICH diagnosis was established in 302 preterms (20.4 %). The early mortality rate was 3.3%: from the total study group of 302 preterms, 10 died between the first 5-7 days following admission. The remaining 292 newborns diagnosed with ICH were subjected to the follow-up study according to the above mentioned common examination protocol.

The demographic characteristic of the study group (295 newborns) are summarized in table I.

The first head ultrasound was performed between postnatal day 3 and 8, with a mean of 4.5 days. The variations in TF examination timing was determined by several factors such as the baby condition immediately after birth or postdelivery complications.

The types of intracranial hemorrhage detected by TF ultrasonography (fig 1-5) and neurological sequels associated with ICH are summarized in table II.

Table I. Study group characteristics (n=292)

Characteristics	
Mean age at the first TF examination	4.5 days
Sex ratio M:F	184 (63%) : 108(37%)
Vaginal delivery/caesarian section	192 (65,75 %)/100 (34,25 %)
Apgar score at 1 minute	
<5	11%
5-7	37%
8-10	38%
not recorded	14%
Gestational age	
37-35 w	24.41% (72)
35-32 w	30.14% (88)
< 32 w	45.5% (132)

TF-transfontanelar, w-weeks

Table II. The types of intracranial hemorrhage an neurological sequels associated to intracranial hemorrhages

Type of intracranial hemorrhage	Minimal neurological sequels*	Major neurological sequels **	p value
Grade I, subependimal hemorrhage (n=102)	9 (8, 82 %)	0	**<0,05**
Grade II intraventricular hemorrhage (n=84)	12 (14, 28 %)	0	**<0,05**
Grade III intraventricular hemorrhage (n=40)	9 (22, 5 %)	7 (17, 5 %)	NS
Grade IV parenchymal hemorrhage (n=29)	6 (20, 6 %)	20 (68, 96 %)	**<0,05**
Cerebellar hemorrhage (n=12)	2 (16, 66 %)	8 (66, 66 %)	**<0,05**
Thalamic hemorrhage (n=8)	4 (50%)	3 (37, 5%)	NS
Subarahnoidian hemorrhage (n=6)	2 (40 %)	0	NS
Subdural hemorrhage (n=11)	5 (45, 45 %)	3 (27, 27 %)	NS

* Minimal neurological sequels: mild motor retardation, mild speech and language delay
** Major neurological sequels: cerebral palsy, sensorial dysfunctions (visual and/or auditive), mental retardation, motor retardation, epilepsy.

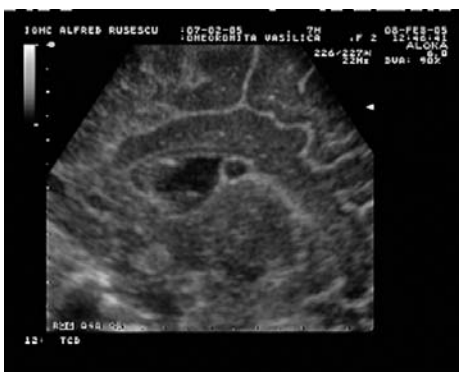

Fig 1. Sagital view: grade I – subependymal hemorrhage: cyst at the thalamo-caudate groove level

Fig 3. Coronal view: grade IV – intraventricular hemorrhage with massive echogenic clot inside the left lateral ventricle. Asymmetrical ventriculomegaly.

Fig 2. Sagital view: grade II hemorrhage with moderate left ventriculomegaly

Fig 4. Coronal view: hydrocephalus secondary intraventricular hemorrhage

Fig 5. Sagital view: periventricular leucomalacia secondary to severe hypoxia in preterm.

Discussions

The study's main objective was to determine the prevalence and proportion of the main types of ICH diagnosed by TF ultrasound among admitted preterms over a 5 year period. The second endpoint of the study was a neuro-developemental assessment on a 12 month follow-up for those babies diagnosed with brain injury at birth. The prevalence of all types of ICH for a 5 years period was 20.4 % on a cohort of 1480 examined preterms. According to literature data, the incidence of peri and intraventricular hemorrhages widely ranges from 5% to 90%, depending on the type of study population [10,11]. Although the study cohort was relatively small, the observed 20.4% prevalence is in line with most literature data regarding ICH in premature babies.

The following potential risk factors for ICH taken into account in the study group will be discussed in the above section: gender, delivery type, Apgar score and gestational age.

As outlined by several studies, ICH are more frequent in males compared to females, especially in those prematures with a low birth weight (<1500 g). Amato et al found a 2.5 higher prevalence in low birth weight males, compared to females [12]. A more recent study confirms this observation and demonstrates that even in the modern era of neonatology, the male infant mortality remains higher along with the long-term neurologic poor prognosis. According to the same study, gender differences tend to to lose significance at 27 weeks gestation [13]. A possible explanation of the male predisposition to ICH relies in their relative delay in the cerebral vascular maturation leading to a difference in the risk of developing ICH [8,14]. In our study, we demonstrated a 1.7 higher frequency of ICH in all preterm males. Although the prevalence is not as high as in the above-mentioned study, this observation confirms the already described vulnerability of premature males for this type of complication.

In our study, more than half of the preterms were vaginally delivered, with a higher incidence of ICH, compared with those born by caesarian section, as also demonstrated by Shankaran et al [15] which described a 2.9 higher risk in the first group. However, other observations tend to bring different data on this relationship. Studies performed on very low birth weight babies, found that the outcome was improved by a lower risk of ICH in those deliverd vaginally, compared to caesarian section [16,17].

The relationship between the type of delivery and the occurrence of perinatal ICH seems to depend on several factors, the gestational age being considered of major significance [18].

Perinatal hypoxia is supposed to be one of the most important determinants in the preterm's ICH etiology, as confirmed by several reports [19,20]. The relationship between a low Apgar score at 1 and 5 minutes and the risk of developing ICH is already well documentated [20,21]. The Apgar score proved to be a good prognostic factor, particularly at 1 and 5 minutes after birth [22]. The Apgar score at 1 minute in the study group was less than 7 in 41.28% of the preterms diagnosed with various types of ICH. An inverse relationship between the Apgar score at 1 and 5 minutes and both the incidence and severity of ICH in the study group was also noticed. According to most literature data, the prematurity is known to predispose to intracranial hemorrhages [19,20]. The most important way of preventing neurological damage in infants is to increase gestational age at birth and by this to avoid the intraventricular haemorrhage and periventricular leukomalacia [23].

In our study the babies with a gestational age of less than 32 weeks represented almost half of the group. Literature reviews and published studies [24,25,26] demonstrate the direct relationship between the degree of prematurity and the increased ICH risk. It is generally accepted that the incidence and severity of the ICH is related to both gestational age and birth weight, occurring in 25-30% of patients born at less than 32 weeks gestation, with less than1500g [27]. However, in several reports the intracranial hemorrhage prevalence in all gestational ages preterms is much more higher, between 40-45% [28].

On the study cohort of 1480 preterms almost one quarter were diagnosed with one type ICH. The most prevalent were the peri and intraventricular hemorrhages, classified on the Papile and Volpe 4 degrees scale, according to their location and severity. Usually, with respect to the neurological outcome, the peri and intraventricular

hemorrhages are grossly classified in mild to moderate (grade I and II) and severe (grade III and IV).

In the study group, grade I – subependimal hemorrhages represented 40 % of the ICH. Most literature data demonstrate a lower incidence (around 20 %) of grade I hemorrhages in the preterm [28]. Because the TF examinations were performed acording to a standardized protocol, the risk of over-diagnosing was minimal, however, no complete explanation regarding the high percentage of grade I hemorrhages could be found. In the majority of cases, the subependimal hemorrhages were incidental findings, with no suggestive clinical symptoms. Subjects with subependimal hemorrhages generally demonstrated a good prognosis, as confirmed by several liteature reports [29], although a few studies observed that even in the absence of neuroimaging abnormalities, the very low birth weights infants have a higher incidence of cognitive and behavioral disabilities which might persist into adolescence and adulthood [30]. In our study, minimal neurological sequels were observed in 8% of cases and no major neurological disabilities were noticed on the 12 month follow-up. The correlation between grade I – subependimal hemorrhages and the overall good neurological outcome was found statistically significant ($p < 0.05$) in the study group. The subjects diagnosed with a grade II intraventricular hemorrhage demonstrated a similar pattern with the previous group, although the percent of minor neurological sequels was slightly higher. No major neurodevelopemental problems were observed in the 12 month follow-up. This relationship was either statistically significant ($p<0,05$) in our study. According to most reported data, both grades I and II peri-intraventricular hemorrhages tends to have low/moderate long-term impact on the cognitive and neuromotor development of the baby. [31-33].

On the contrary, the more severe grade III and IV hemorrhages are associated with a poor developmental prognosis [33]. In our group the neurological sequels were mostly associated to intraventricular grade III and IV ICH, with / or without periventricular white matter lesions (periventricular leukomalacia - PVL) or post hemorrhagic hydrocephalus. Grade III hemorrhage was associated to severe neurological sequels in 17,5 %. Grade IV parenchymal hemorrhage was characterized by an overall severe outcome with 89.56 % sequels: 20,6 % minor disabilities and 68,96 % major neurological dysfunctions. The correlation was found to be statistically significant ($p<0,05$) only for grade IV hemorrhages. Several reports reveal 57-80% severe neurological sequels in subjects with a grade IV hemorrhage and 10-20 % in grade III [14,17,18,34].

Periventricular leukomalacia (PVL) and ventriculomegaly developed after birth are known to be associated with severe cognitive and motor disabilities [33]. PVL represents the most frequent complication of perinatal hypoxia in preterm [35,36]. PVL incidence in preterms admitted in the intensive care units varies between 4-26%, and postmortem examination demonstrates a much higher incidence of around 75% [37,38]. PVL associated to intraventricular hemorrhage is typically found in extreme prematurity or in severe perinatal hypoxia [35,36]. We found a prevalence of PVL similar to the existing data in the literature. A direct relationship between the presence of PVL and the severity of neurological sequels was also observed.

According to the literature, various degrees of post hemorrhagic hydrocephalus might complicate the grade II, III or IV intraventricular hemorrhages in overall 70% of cases [39,40]. In this study post hemorrhagic hydrocephalus was only observed only in some of the subjects with a grade III and IV.

Patients diagnosed with cerebellar and thalamic hemorrhages are generally associated with a severe neurological outcome [41]. Our study data were statistical significant ($p<0.05$) only for the cerebellar hemorrhage outcome. Although in the study group subdural hemorrhage associated 45,45 % minor and 27,27 % major neurological sequels, and subarahnoid only 40% minor dysfunctions, no statistical significance could be established for both.

There are several limitations of our study, the most important being the lack of data on the late outcome of prematurity (follow-up until at least 6 years of age), along with the relatively small number of cases. Although early brain damage secondary to ICH is nevertheless very important, neuro-psycho-motor development in humans is multifactorial determined, making sometimes the assessment difficult. The role of subtle white matter injury that cannot be detected by TF ultrasound but only with MRI requires further investigation .

Conclusions

Although long-term neurological impairment is not always present, it is beneficial to understand the prevalence and mechanisms of brain injury associated to prematurity, in order to anticipate the long-term developemental problems of this babies.

The lack of any specific treatment of the preterm ICH apparently limitate the screening studies to research purposes. However, systematic TF screening proved to be useful for early diagnosis and staging, providing appropriate information for early stage prevention strategy, improving the management of rehabilitation therapies and influencing the quality of parental counseling.

This analysis demonstrates once again that prematurity represents a significant health problem, not only in terms of associated mortality but also by the short- and long-term sequels determining a major burden for the health-care system.

Conflict of interest: none

References

1. Amess P, McFerran C, Khan Y, Rabe H. Early prediction of neurological outcome by term neurological examination and cranial ultrasound in very preterm infants. Acta Paediatr 2009; 98: 448-453.
2. Routine screening cranial ultrasound examinations for the prediction of long term neurodevelopmental outcomes in preterm infants. Paediatr Child Health 2001; 6: 39-52.
3. Oh W, Fanaroff AA, Verter J, et al. Neonatal mortality and morbidity in very low birth weight (VLBW) infants: a seven-year trend analysis of the Neonatal Research Network data. Pediatr Res 1996; 39: 235A.
4. Ancel PY, Livinec F, Larroque B, et al; the EPIPAGE Study Group. Cerebral palsy among very preterm children in relation to gestational age and neonatal ultrasound abnormalities: the EPIPAGE cohort study. Pediatrics 2006; 117; 828-835.
5. Krishnamoorthy KS, Kuban KC, O'Shea TM, et al; ELGAN Study Co-investigators. Early cranial ultrasound lesions predict microcephaly at age 2 years in preterm infants. J Child Neurol 2011; 26: 188-194.
6. Surveillance of cerebral palsy in Europe: a collaboration of cerebral palsy surveys and registers. Surveillance of Cerebral Palsy in Europe (SCPE). Dev Med Child Neurol 2000; 42: 816-824.
7. Beck S, Wojdyla D, Say L, et al. The worldwide incidence of preterm birth: a systematic review of maternal mortality and morbidity. BullWorld Health Organ 2010; 88: 31-38.
8. Papile LA, Burstein J, Burstein R, Koffler H. Incidence and evolution of subependymal and intraventricular hemorrhage: a study of infants with birth weights less than 1500 g. J Pediatr 1978; 92: 529–534.
9. Volpe JJ. Intracranial hemorrhage: germinal matrix-intraventricular hemorrhage of the premature infant: neurology of the newborn. Philadelphia: W.B. Saunders 1995: 403–462.
10. Miranda P. Intraventricular hemorrhage and posthemorrhagic hydrocephalus in the preterm infant. Minerva Pediatr 2010; 62: 79-89.
11. Patra K, Wilson-Costello D, Taylor HG, Mercuri-Minich N, Hack M. Grades I-II intraventricular hemorrhage in extremely low birth weight infants: effects on neurodevelopment. J Pediatr 2006; 149: 169-173.
12. Amato M, Howald H, von Muralt G. Incidence of peri-intraventricular hemorrhage in premature neonates weighing more than 1500 g. J Perinat Med 1987; 15: 91-94.
13. Kent AL, Wright IM, Abdel-Latif ME; New South Wales and Australian Capital Territory Neonatal Intensive Care Units Audit Group. Mortality and adverse neurologic outcomes are greater in preterm male infants. Pediatrics 2012; 129: 124-131.
14. Tioseco JA, Aly H, Essers J, Patel K, El-Mohandes AA. Male sex and intraventricular hemorrhage. Pediatr Crit Care Med 2006; 7: 40-44.
15. Shankaran S, Bauer CR, Bain R, Wright LL, Zachary J.Prenatal and perinatal risk and protective factors for neonatal intracranial hemorrhage. National Institute of Child Health and Human Development Neonatal Research Network. Arch Pediatr Adolesc Med 1996; 150: 491-497.
16. Bauer J, Hentschel R, Zahradnik H, Karck U, Linderkamp O. Vaginal delivery and neonatal outcome in extremely-low-birth-weight infants below 26 weeks of gestational age. Am J Perinatol 2003; 20: 181-188.
17. Velisavljev-Filipović G. Mode of delivery and neurosonographic findings in premature infants. Med Pregl 2007; 60: 7-11.
18. Baumert M, Brozek G, Paprotny M, et al. Epidemiology of peri/intraventricular haemorrage in newborns at term. J Physiol Pharmacol 2008; 59 Suppl 4: 67–75.
19. Stevenson DK, Benitz WE, Sunshine P, Hintz SR, Druzin MJL. (Eds.). Fetal and Neonatal Brain Injury. Fourth Edition. Cambridge University Press 2009: 202-207.
20. Sarkar S, Bhagat I, Dechert R, Schumacher RE, Donn SM. Severe intraventricular hemorrhage in preterm infants: comparison of risk factors and short-term neonatal morbidities between grade 3 and grade 4 intraventricular hemorrhage. Am J Perinatol 2009; 26: 419-424.
21. Berger R, Bender S, Sefkow S, Klingmüller V, Künzel W, Jensen A. Peri/intraventricular hemorrhage: a cranial ultrasound study on 5286 neonates. Eur J Obstet Gynecol Reprod Biol 1997; 75: 191-203.
22. Jaeger M, Grüssner SE, Omwandho CO, Klein K, Tinneberg HR, Klingmüller V. Cranial sonography for newborn screening: a 10-year retrospective study in 11,887 newborns. Rofo 2004; 176: 852-858.
23. Vermeulen GM, Bruinse HW, de Vries LS. Perinatal risk factors for adverse neurodevelopmental outcome after spontaneous preterm birth. Eur J Obstet Gynecol Reprod Biol 2001; 99: 207-212.
24. Linder N, Haskin O, Levit O, et al. Risk factors for intraventricular hemorrhage in very low birth weight premature infants: a retrospective case-control study. Pediatrics 2003; 111: e590-595
25. Gleissner M, Jorch G, Avenarius S. Risk factors for intraventricular hemorrhage in a birth cohort of 3721 premature infants. J Perinat Med 2000; 28: 104–110.
26. Oh W, Fanaroff AA, Verter J, et al. Neonatal mortality and morbidity in very low birth weight (VLBW) infants: a seven-year trend analysis of the Neonatal Research Network data. Pediatr Res 1996; 39: 235A.
27. Harris DL, Teele RL, Bloomfield FH, Harding JE; Australian and New Zealand Neonatal Network. Does variation in interpretation of ultrasonograms account for the variation in incidence of germinal matrix/intraventricular hemorrhage between newborn intensive care units in New Zealand? Arch Dis Child Fetal Neonatal Ed 2005; 90: F494–F499.

28. Kadri H, Mawla AA, Kazah J. The incidence, timing, and predisposing factors of germinal matrix and intraventricular hemorrhage (GMH/IVH) in preterm neonates. Childs Nerv Syst 2006; 22: 1086-1090.
29. Bassan H. Intracranial hemorrhage in the preterm infant: understanding it, preventing it. Clin Perinatol 2009; 36: 737-762.
30. Roland EH, Hill A. Germinal matrix-intraventricular hemorrhage in the premature newborn: management and outcome. Neurol Clin 2003; 21: 833-851.
31. Volpe JJ. Neurobiology of periventricular leukomalacia in the premature infant. Pediatr Res 2001; 50: 553-562.
32. Looney CB, Smith JK, Merck LH, et al. Intracranial hemorrhage in asymptomatic neonates: prevalence on us images and relationship to obstetric and neonatal risk factors. Radiology 2007; 242: 535-541.
33. Gardner MR. Outcomes in children experiencing neurologic insults as preterm neonates. Pediatr Nurs 2005; 31: 448, 451-456.
34. O'Shea TM, Allred EN, Kuban KC, et al; ELGAN Study Investigators. Intraventricular hemorrhage and developmental outcomes at 24 months of age in extremely preterm infants. J Child Neurol 2012; 27: 22-29.
35. Blumenthal I. Periventricular leucomalacia: a review. Eur J Pediatr 2004; 163: 435-442.
36. Liu J, Li J, Qin GL, Chen YH, Wang Q. Periventricular leukomalacia in premature infants in mainland China. Am J Perinatol 2008; 25: 535-540.
37. Scher MS. Fetal and neonatal neurologic case histories: assessment of brain disorders in the context of fetal-maternal-placental disease. Part 1: Fetal neurologic consultations in the context of antepartum events and prenatal brain development. J Child Neurol 2003; 18: 85-92.
38. Fawer CL, Calame A, Perentes E, Anderegg A. Periventricular leukomalacia: a correlation study between real-time ultrasound and autopsy findings. Periventricular leukomalacia in the neonate. Neuroradiology 1985; 27: 292–300.
39. Persson E K, Hagberg G, Uvebrant P. Hydrocephalus prevalence and outcome in a population-based cohort of children born in 1989-1998. Acta Paediatr 2005; 94: 726-732.
40. Treatment of Childhood Hydrocephalus at Mayo Clinic in Rochester, 2005. Available at URL: http://www.mayoclinic.org/peds-hydrocephalus-rst/
41. Vannucci R. Hypoxic–ischemic encephalopathy. Am J Perinatol 2000; 17: 113–120.