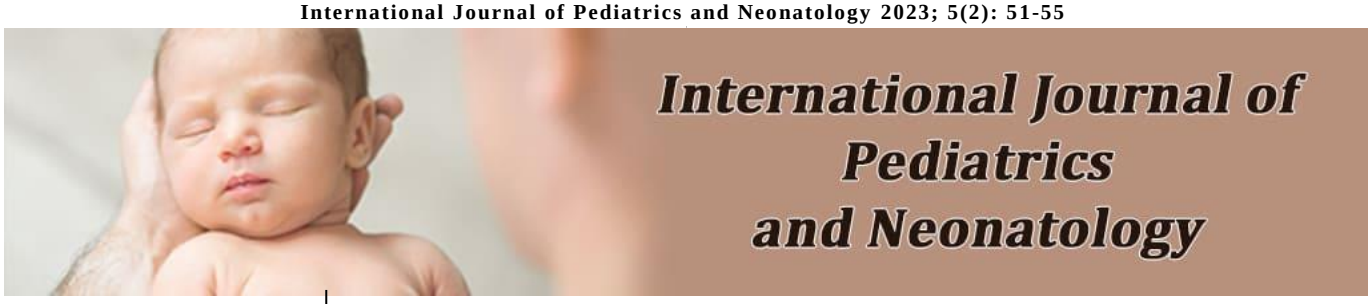

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Ultrasonographic Evaluation of Brain of Newborn with Hypoxic- Ischaemic Encephalopathy Treated With Anticonvulsant Drug

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Abstract
Introduction: The most serious consequence of perinatal asphyxia is hypoxic-ischemic encephalopathy (HIE) which causes permanent damage to CNS tissues that may result in neonatal death or manifest later as cerebral palsy or developmental delay. Despite major advances in fetal and neonatal care, hypoxic ischemic encephalopathy (HIE), sometimes called perinatal encephalopathy, continues to cause a significant number of deaths and bong-term disabilities in newborns. Cranial ultrasonography (CUS) in neonates is safe and radiation free. CUS can be initiated even immediately after birth and hence suitable for screening. This investigation is chosen as a tool to detect any early changes that might be a significant predictor of future neurological outcome.
Objective: This study was done to identify the ultrasonographic findings of brain of newborn with hypoxic- ischaemic encephalopathy.
Methods: A cross sectional study was conducted for ultrasonographic evaluation of brain of newborn with hypoxic ischemic encephalopathy treated with anticonvulsant drug. In this cross sectional study, total 100 neonates were selected according to selection criteria. Parents were interviewed with a specific pre-designed and pre-tested questionnaire and some information was gathered by reviewing the document and observation. Collected data were cleaned, edited and analyzed with the help of software SPSS 17.
Results: Among the study subjects majority were delivered within 40 weeks (55.0%) More than one third was delivered within ≥40 weeks (45.0%) More than half of the study subjects were male (63.0%). Average age was 13.6±2.6 (SD) and average birth weight was 2632±94.56 (SD) More than two third of the study subjects had delayed cry after birth (88.0%) and no cry less than one third (12.0%). Respiratory distress was found (66.0%) cases. Half of the subjects had bluish coloration after birth (50.0%). All the patients had convulsion after birth. Majority of the study subjects were lethargic (43.0%). More than one third was in coma (35.0%). Twenty two percent were hyper alert (22.0%). Nearly one third of the study subjects had good activity (30.0%) and good reflexes (31.0%). Majority of the study subjects were hypotonic (70.0%). Hypertonic were 20.0%. Only 10.0% were normal. Less than one third of the study subjects had no HIE (30.0%). Majority of the study subjects were in stage II HIE (67.0%). Stage III and Stage I HIE were found 20.0% and 13.0% cases respectively. Among the study subjects, normal finding in cranial USG was found for 65 (65.0%). Dilatation of the ventricle was found in (15.0%) cases. Periventricular leukomalacia and Intraventricular haemorrhage were 12.0% and 8.0% respectively. No cerebral oedema was detected.
Conclusion: Cranial ultrasonography is the most widely used technique for evaluating brain morphology and cerebral lesions in neonates. USG of brain can detect several abnormalities like dilatation of the ventricles, intraventricular haemorrhage and periventricular leukomalacia in newborn which can lead to fatal neurological outcome in future. These cases are important candidates for early intervention to maximize a better outcome. So this test can be helpful for identification of vulnerable groups and counseling of the parents.

Keywords: Ultrasonographic, Newborn, Hypoxic- Ischemic, Encephalopathy

Introduction
The most serious consequence of perinatal asphyxia is Hypoxic-ischaemic encephalopathy (HIE) which causes permanent damage to CNS tissues that may result in neonatal death or manifest later as cerebral palsy or developmental delay.

About 20-30% of infant with HIE die in the neonatal period, and 33-50% of survivors are left with permanent neurodevelopmental abnormalities (cerebral palsy, mental retardation) [1]. In a study HIE was found to be the commonest etiology of seizure (56.4%). Among the HIE cases, 31.9% were with stage II and 3.2% were with stage III and others were complicated with septicaemia [2]. Perinatal asphyxia and its consequences account for approximately one third of early neonatal death and is the leading cause of under-five mortality. To achieve the Millennium Development Goal 4 (MDG 4) under five, mortality is to be reduced by two third by the year 2015. The burden of death in neonatal period alone adversely influences MDG 4 target [3]. Despite major advances in fetal and neonatal care, hypoxic ischemic encephalopathy (HIE), sometimes called perinatal encephalopathy, continues to cause a significant number of deaths and long-term disabilities in newborns. The neurologic changes associated with HIE may be brief, lasting only a few minutes to hours, or may be permanent. Generally, the longer an infant goes with low blood flow or low oxygen, the more severe or permanent the injury [4]. Perinatal asphyxia or hypoxic-ischemic encephalopathy (HIE) is a condition of impaired blood gas exchange during the intrapartum period that, if it persists, leads to progressive hypoxemia with a metabolic acidosis. HIE is a subset of neonatal encephalopathy [5]. The newborn's body can compensate for brief periods of depleted oxygen, but if the asphyxia lasts too long, brain tissue is destroyed. Hypoxic-ischemic encephalopathy due to fetal or neonatal asphyxia is a leading cause of death or severe impairment among infants. Such impairment can include epilepsy, developmental delay, motor impairment, neurodevelopmental delay, and cognitive impairment. Usually, the severity of impairment cannot be determined until a child is three to four year old [6]. In many cases, the exact cause is not known. In some infants, lack of blood flow or oxygen may occur before, during or shortly after a baby's birth. Particular roles for increase in extracellular glutamate, excessive activation of glutamate receptors (Excitotoxicity), increase in cytosolic calcium (Ca2+), and generation of free radicals are emphasized. The temporal aspects of the changes in glucose and energy metabolism after HI insult have been identified and include primary energy failure and secondary energy failure [7]. The occurrence of secondary energy failure varies according to species and nature of the insult with onset at appropriately 8-16 hours and a nadir at 24-48 hours. High-energy phosphate levels recovered to baseline levels in 2-3 hours after reperfusion and reoxygenation, and a second decline in high- energy phosphate were pronounced at the next 48 hours [7-9]. According to World Health Organization estimates, in the developing countries 3% of all infants (3.6millions) suffer from moderate to severe birth asphyxia, of which 23% (840,000) die and approximately the same number develop serious sequelae [10]. There are few epidemiological data on HIE in Bangladesh. One study carried out in Dhaka Medical College Hospital and incidence of birth asphyxia was from 29% to 36% and HIE among them was (45%) and mortality among them were around 25% [11]. The presence of seizure, within the first hour, predicates a poor outcome of HIE. The energy metabolism can be compromised by the hyperactive neurons, and both acute energy deprivation after HI insult and seizures are implicated in excitotoxicity. Thus, the therapeutic value of antiepileptic drugs (AEDS) may include not only control of seizure activity but also potentially the benefit for the compromised cellular energy metabolism. Studies about perinatal HIE showed a beneficial effect of pretreatment with anticonvulsant drugs [12]. Phenobarbital remains the preferred drug for the treatment of seizures in neonates with HIE [13]. Cranial ultrasonography (CUS) in neonates is safe and radiation free. Safety of sonography is well established in fetuses and infants except for Trans cranial Doppler where there can be local rise of tissue temperature and cavitation if performed for longer duration. CUS can be easily performed at the bedside. CUS can be initiated even immediately after birth and hence suitable for screening. It can be repeated as often as possible without any adverse effects and hence helps in proper follow up of babies with neurological problems. Lastly, CUS is a significantly cheaper modality of neuroimaging compared with other techniques [14]. Several studies have been done to find out the incidence and pattern of changes of brain in neonate with HIE but still it remains a challenge to reduce the neonatal mortality. Ultrasonogram which is safe, less costly, radiation free, easily available in most of the facilities of our country. So this investigation is chosen as a tool to detect any early changes that might be a significant predictor of future neurological outcome. This study was done to identify the ultrasonographic findings of brain of newborn with hypoxic- ischaemic encephalopathy.

Materials and Methods

Study Design: Cross Sectional study.

Study Place: Department of Pediatrics, Sir Salimullah Medical College Mitford Hospital, Dhaka, Bangladesh.

Study Duration: April 2015 to September 2015 (6 month).

Study Population: Newborn with hypoxic- ischemic encephalopathy admitted in neonatal care unit of SSMC&MH during study period.

Inclusion Criteria

1. Babies with HIE treated with anticonvulsant drug. (Phenobarbitone, Phenytoin, Fosphenytoin).
2. Babies with 37 completed weeks of gestation.
3. Post natal age of babies >3 days.

Exclusion Criteria

1. Preterm babies.
2. Babies with low birth weight <2500 gm.
3. Those with congenital anomalies

Sample Size Calculation

$$n = \frac{pqZ^2\, pqN}{e^2\,(N-1)+Z^2\, pq}$$

=278 (approximately)

So, Calculated Sample size was 278

But due to time constrain and unavailability of cases, this study enrolled 100 cases.

Operational Definition: Hypoxic-ischemic encephalopathy (HIE) was defined clinically on the basis of difficulty with

initiating spontaneous respiration at birth with subsequent seizure in term newborn.

Procedure of Data collection: Newborn with hypoxic-ischemic encephalopathy admitted in neonatal care unit of SSMC&MH fulfilling the inclusion and exclusion criteria were enrolled in this study. After informed consent from the parents, detailed history was taken by using preset questionnaire. Age, Sex, socioeconomic and residence status was evaluated from history sheet, discharge paper and documented investigation result sheet. USG of brain was done on 4th day of admission by expert sinologist ranking assistant professor and above in the department of radiology & imaging of this hospital. Rechecking of all cases was not possible in our settings but in doubtful cases consultation was done with senior professors. In case of non-affordable patient institutional support was arranged by the researcher. Findings of history, physical examination, investigations and follow up were recorded in the record form.

Data Analysis: Data were processed and analyzed by using computer software SPSS (Statistical Package of Social Science) Version 17.

Results

Table 1: Distribution of the study subjects according to gestational age (N=100)

Gestational age (in wks.)	No. of the study subjects	Percentage (%)
37 to <40 week	55	55.0
40 to <42 week	45	45.0
Total	100	100.0

A total 100 neonates were selected according to selection criteria. Parents were interviewed with a specific pre-designed and pre-tested questionnaire and some information was gathered by document review and observation. Among the study subjects majority were delivered within 40 weeks (55.0%). More than one third was delivered within ≥40 weeks (45.0%) (Table-1).

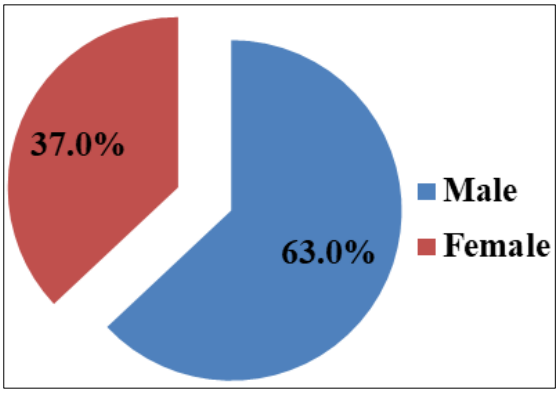

Fig 1: Distribution of the study subjects according to sex.

More than half of the study subjects were male (63.0%) and rest were female (37.0%) (Fig-1).

Table 2: Age and birth weight of the study subjects on admission (N=100)

Characteristics	Mean± SD	Minimum	Maximum
Age (in hours)	13.6±2.6	11.5	17
Birth weight (in gm.)	2632.06±94.56	2500	2800

Average age was (13.6±2.6 (SD) and average birth weight was 2632.06±94.56 (Mean ±SD) (Table-2).

Table 3: Presenting symptoms of the study subjects (N=100)

Presenting Symptoms	Frequency(n)	Percent (%)
Delayed cry	88	88.0
No cry	12	12.0
Bluish coloration after birth	50	50.0
Respiratory distress	66	66.0

More than two third of the study subjects had delayed cry after birth (88.0%) and no cry less than one third (12.0%). Respiratory distress was found (66.0%) cases. Half of the subjects had bluish coloration after birth (50.0%) (Table-3).

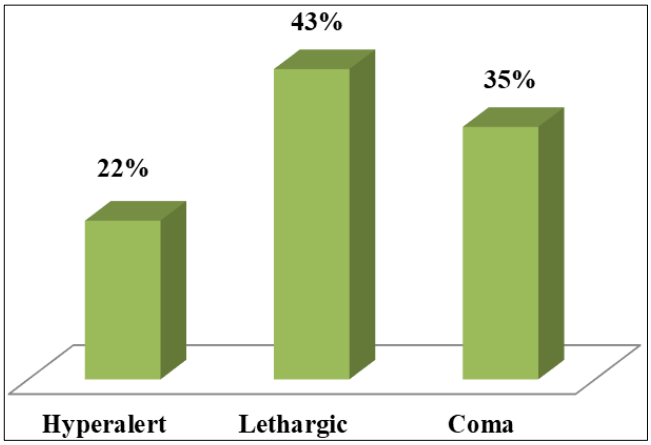

Fig 2: Level of consciousness among the study subjects.

Fig-2 shows that, majority of the study subjects were lethargic (43.0%). More than one third was in coma (35.0%). Twenty two percent were hyper alert (22.0%).

Table 4: Activity and reflex of the study subjects (N=100)

Characteristics	Good n (%)	Poor n (%)
Activity	30 (30.0)	70(70.0)
Reflex	31(31.0)	69(69.0)

Table-4 shows that, nearly one third of the study subjects had good activity (30.0%) and good reflexes (31.0%).

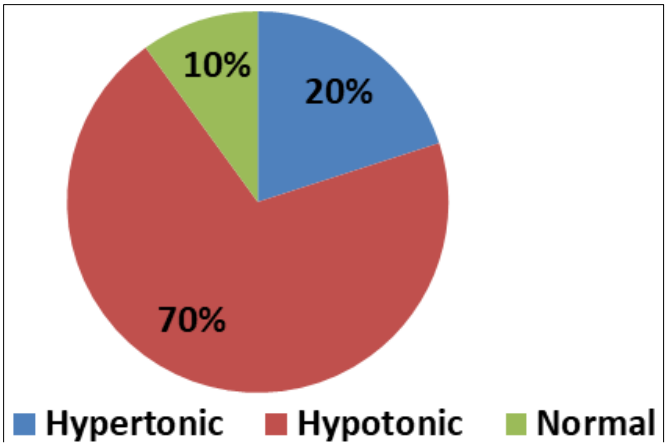

Fig 3: Condition of the muscle tone of the study subjects.

Fig-3 shows that, majority of the study subjects were hypotonic (70.0%) Hypertonic were 20.0% only 10.0% were normal.

Table 5: Distribution of HIE among the study subjects (N=100)

HIE	No. of the study subjects	Percentage (%)
Stage I	13	13.0
Stage II	67	67.0
Stage III	20	20.0
Total	100	100.0

Table-5 shows that, majority of the study subjects were in stage II HIE (67.0%). Stage III and Stage I HIE were found 20.0% and 13.0 % cases respectively.

Table 6: Cranial USG findings of the study subjects (N=100)

Findings	No. of the study subjects	Percentage (%)
Normal study	65	65.0
Dilatation of the Ventricle	15	15.0
Periventricular leukomalacia	12	12.0
Intraventricular haemorrhage	8	8.0
Cerebral oedema	00	00
Total	100	100.0

Among the study subjects, normal finding in cranial USG was found for 65 (65.0%). Dilatation of the ventricle was found (15.0%) cases (Table-6). Periventricular leukomalacia and Intraventricular haemorrhage were 12.0% and 8.0% respectively. No cerebral oedema was detected. Though CUS is cheap, non-invasive procedure but CUS as well as CT, is of limited use in the detection of superficial cortical and subcortical zone injuries. MRI imaging is the modality of choice in term infants who experience partial asphyxial events which is more effective to identify these lesions.

Discussion

A cross sectional study was conducted for ultrasonographic evaluation of brain of newborn with hypoxic- ischemic encephalopathy treated with anticonvulsant drug in Sir Salimullah Medical College & Mitford Hospital, Dhaka. Apgar scoring system, despite some limitations, is widely used throughout the world to diagnose birth asphyxia. But in this study, it was not taken into account. Among the study subjects majority were delivered within 40 weeks (55.0%). More than one third was delivered within ≥40 weeks (45.0%). In this study more than half of the study subjects were male (63%) and the male, female ratio was 63:37 (Nearly 3:2) which nearly approaches other studies [15-18]. Average age was 13.6±2.6 hours (SD) and this can be explained as that, the asphyxiated baby developed multiple complications at an earlier age and needed early admission. In this study average birth weight was 2632±94.5 gm. (SD) which is similar to the findings of Goldberg [19]. In another study conducted by Shireen N et al., and found that mean age of study subjects was 13.8hours which was similar findings in my study [20]. More than two third of the study subjects had delayed cry after birth (88.0%) and no cry less than one third (20.0%). Respiratory distress was found (66.0%) cases. Half of the subjects had bluish coloration after birth (50.0%). Majority of the study subjects were lethargic (43.0%). More than one third was in coma (35.0%). Twenty two percent were hyper alert (22.0%). Nearly one third of the study subjects had good activity (30.0%) and good reflexes (31.0%). Majority of the study subjects were hypotonic (70.0%). Hypertonic were 20.0%. Only 10.0% were normal. Majority of the study subjects were in stage II HIE (67.0%). Stage III and Stage I HIE were found 20.0% and 13.0% cases respectively. Among the study subjects, normal finding in cranial USG was found for 65 (65.0%). Dilatation of the ventricle was found (15.0 %) cases. Periventricular leukomalacia and Intraventricular haemorrhage were 12.0% and 8.0% respectively. No cerebral oedema was detected. It means that though 65% showed normal cranial ultrasonography, 35.0% developed some sort of neurological complication during hospital stay. A study was done by Mercuri E et al., found that ultrasound abnormalities were present in 20% cases. Ischaemic lesions, such as periventricular and thalamic densities were the most common finding (8%), followed by haemorrhagic lesions (6%). The possible sequelae of antenatal haemorrhages, such as focal ventricular dilatation or choroid cysts, were present in 6%. The findings of ventricular dilatation by USG in that study are almost similar in my study [18]. Cranial ultrasonography is the most widely used technique for evaluating brain morphology and cerebral lesions in neonates. Serial ultrasound scans can identify not only the presence of lesions but also their type and extent. Ultrasound scanning is cheap, easy to perform, non-invasive and easily repeatable, and it has become a routine procedure in neonatal intensive care, and in particular in all the infants who are at risk for brain lesions. Many studies have been performed in preterm infants and these have provided important information on the incidence and evolution of cerebral lesions and their relation with gestational age. Cranial ultrasonography has also been widely used in full term infants, but mainly in those who are at risk of brain lesions, such as those with birth asphyxia or abnormal neurological signs [21-25].

Conclusion

Cranial ultrasonography is the most widely used technique for evaluating brain morphology and cerebral lesions in neonates. USG of brain can detect several abnormalities like dilatation of the ventricles, Intraventricular haemorrhage and periventricular leukomalacia in newborn which can lead to fatal neurological outcome in future. These cases are important candidates for early intervention to maximize a better outcome. So this test can be helpful for identification of vulnerable groups and counseling of the parents.

Recommendation

- When planning therapeutic approaches for hypoxie ischaemic encephalopathy neonates, development of neurological sequelae always should be taken into consideration and identification and treatment of it should be an integral part of management protocol.
- Primary care physicians should be informed about the immediate outcome in perinataly asphyxiated neonate and should get proper training to calculate the stage of HIE and correction of these complications ensure improved quality of life and reduce morbidity and mortality among them.
- Cranial ultrasonographic findings should in consideration onwards and appropriate planning of therapy to correct them accordingly. Individual patient should be taken as an individual case.
- Integrated approach should be taken for their effective management.

- Further in depth research should be conducted to clarify the cranial ultrasonographic findings and immediate outcome in perinatal asphyxiated neonate and their risk factors.

Limitations of the study

- The study population might not represent the whole community.
- There might be selection bias.
- Due to time and resource limitation sample size was small; a larger sample size would have given a better result.

Source of Funding: Nil.

Conflict of Interest: None.

References

1. Waldemar AC. Nervous system disorder. In: Kliegman RM, Behrman RE, Jenson HB, Stanton BF. editors. Nelson Text Book of Paediatrics. 19th ed. Philadelphia: Saunders Elsevier; c2012. p. 565-72.
2. Zahid H, Farid A. Cranial ultrasonography findings and immediate outcome of neonates with seizure. DS (Child) H J. 2011;27:72-78.
3. Anthony MDC, Dharma SM. Perinatal asphyxia in less developed countries. Journal of the British Paediatrics Association. 1994;7:1-3.
4. Ann, Robert HL. Children's Hospital of Chicago. Neonatology, Hypoxic Ischemic Encephalopathy. 2014;15:1-8.
5. Gomella TL. A Lange Clinical manual Neonatology. 6th ed. USA: McGraw-Hill; c2009; p. 624.
6. http://www. My child at cerebral palsy.org.html
7. Johnston MV, Trescher WH, Ishida A, Nakajima W, Zipursky A. Neurobiology of hypoxic-ischemic injury in the developing brain. Pediatric Research. 2001;49:735-41.
8. Penrice J, Lorek A, Cady EB. Proton magnetic resonance spectroscopy of the brain during acute hypoxia-ischemia and delayed cerebral energy failure in the newborn piglet. Pediatric Research. 1997;41:795-802.
9. Vannucci RC, Towfighi J, Vannucci SJ. Secondary energy failure after cerebral hypoxic-ischemia in the immature rat. Journal of Cerebral Blood Flow and Metabolism. 2004;24:1090-97.
10. UNICEF, State of the World's Children; c2011. p. 88.
11. Shireen N, Nahar N, Mollah AH. Risk factors and short-term outcome of birth asphyxiated babies in Dhaka Medical College Hospital. Bangladesh J child health. 2009;33:83-89.
12. Evans J, Levene MI, Tsakmakis M. Anticonvulsants for preventing mortality and morbidity in full term newborns with perinatal asphyxia. Cochrane Database of Systematic Reviews; c2007, 3, Article ID CD001240.
13. Volpe JJ. Neurology of the Newborn. 5th ed. Boston: Elsevier; c2008. p. 67.
14. Bracci R, Perrone SN, Buonocore G. The Timing of Neonatal Brain Damage. Biol Neonate. 2006;90:145-55.
15. Tooley J. Perinatal asphyxia. Forfur and Arneils Text book of Pediatrics. 7th ed. Elsevier; c2008. p. 204-7.
16. Shankaran S, Laptook AR, Ehraenkranz RA, Tyson JE, Mc Donald SA, Donovan TF, *et al*. Whole body hypothermia for neonates with hypoxic ischemic encephalopathy. NEJM. 2005;353:1574-84.
17. Russel G, Dear J. Which deliveries require pediatricians in attendance? British Medical Journal. 1984:289:435-36.
18. Scheiner AP. Perinatal asphyxia: factors which predicts developmental outcome. Dev. Med. Child. Neurol. 1980:22:102-4.
19. Goldberg RN. Hyperammonaemia associated with perinatal asphyxia. Paediatrics. 1979;64:336-41.
20. Shireen N. Risk factors, immediate outcome and cranial ultrasonographic findings of birth asphyxiated babies in Dhaka Medical College Hospital; c2005. p. 67-70.
21. Pape KE, Blackwell RJ, Cusick G. Ultrasound detection of brain damage in preterm infants. Lancet. 1979;1:1261-74.
22. Levene MI, Wigglesworth JS, Dubowitz V. Cerebral structure and Intraventricular haemorrhage in the neonate. A real time ultrasound study. Arch Dis Child. 1981:56:416-24.
23. Rennie JM. Neonatal cerebral ultrasound. Cambridge: Cambridge University Press; c1997.
24. Govaert P, De Vries L. An atlas of neonatal brain sonography. Clinics in Developmental Medicine, London: McKeith Press; c1999. p. 141-2.
25. Govaert P. Cranial haemorrhage in the term newborn infant Clinics in Developmental Medicine, London: McKeith Press; c1993. p. 129.

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