Benha Journal of Applied Sciences (BJAS) print: ISSN 2356–9751
Vol. (7) Issue (2) (2022), (31- 36) online: ISSN 2356–976x
http://bjas.journals.ekb.eg

Evaluation of Hypoxic Ischemic Encephalopathy and Congenital Intracranial Lesions in Preterm Using Transcranial Ultrasound and Color Doppler

A.I.Gafar, A.E.Shalan and A.F.Yousef
Radiodiagnosis, Dept., Faculty of Medicine, Benha Univ., Benha, Egypt
E-mail: ahmedgafar971990&gmail.com

Abstract

Background: Cranial ultrasound is a safe imaging modality that does not require sedation and can be performed bedside, it can be repeated as often as necessary because of the lack of ionizing radiation. This study aimed to evaluate the usefulness of transcranial ultrasound and color Doppler in detecting intracranial lesions and congenital brain anomalies in neonatal age group. Methods: This study was performed on 30 neonates, the age ranged between 1 day to 29 days age old, the study group consisted of 17 females and 13 males, from 30 cases in this study 10 cases were discharged ,6 cases were referred to other big hospitals , 4 cases were defaulted,5 cases were dead and 5 cases were on admission for more follow up regularly, the examined patients classified into 6 main groups , the normal cases seen and consists of 11 cases, the traumatic cases seen and consists of 1 patient, the congenital malformations consists of 5 patients, 3 cases were holoprosencephaly , 2 cases were septo-optic dysplasia and one case of cerebellar hypoplasia .the vascular lesions seen and consists of 10 patients 3 cases of Periventricular germinal matrix hemorrhage & 3 cases were periventricular leucomalacia (PVL) and 1 case as aneurysm of vein of Galen and 1 case of extra-axial hemorrhage and 2 cases of brain parenchymal hematomas. Results: Four main Ultrasound approaches were used; anterior fontanel (AF), [additional winows: (posterior fontanel, mastoid (poster lateral) fontanel, temporal approach]. The examined patients can be classified into 6 main groups. A) Normal cases in the study. B) Traumatic cases. Congenital cases: 3 holoprosencephaly, 2 septo-optic dysplasia,1 cerebellar hypoplasia. Sonographic findings of the congenital group. Sonographic Findings of aneurysm of Vein of Galen is seen as Anechoic cyst Shows high vascularity on Doppler, Multiple dilated surrounding feeding vessels and Supratentorial Hydrocephalus. Conclusions: US has been a major advance in the study of neonatal brain, it is portable safe, non-invasive, low cost and highly effective technique that is of considerable value in evaluation of neonatal intracranial disorders and should be included within integrated approach to CNS imaging in the neonates.

Keywords: Hypoxic Ischemic Encephalopathy, Congenital Intracranial Lesions, Preterm, Transcranial Ultrasound, Color Doppler.

1. Introduction

Cranial ultrasound is a safe imaging modality that does not require sedation and can be performed bedside. It can be repeated as often as necessary because of the lack of ionizing radiation [1].

Brain injury continues to be a serious clinical concern and a leading cause of prenatal morbidity and death [2].

One of the major problems in preterm neonates is damage to white matter. This damage involves multifocal necrosis resulting in cystic periventricular leukomalacia (PVL) or a diffuse astrogliosis and loss of myelin-producing oligodendrocytes [3].

PVL commonly coexists with intraventricular hemorrhages, illustrating the pre-myelinating oligodendrocytes' susceptibility [4].

Germinal atrix hemorrhage (GMH) is a frequent finding in the neonatal period. It curs rimarily, but not exclusively, in preterm neonates of very low birth weight [5].

Congenital brain anomalies are also could be seen during the cranial ultrasound screening, such as Dandy-Walker malformation (DWM), Chiari II malformation, agenesis of corpus callosum, Joubert syndrome, lissencephaly (smooth brain) [1].

The development of Doppler ultrasound has been progressing together with the imaging technology, but the fusing of the two technologies in duplex scanning and the consecutive development of color Doppler imaging provided even more possibility for investigating transmission and blood supply to the brain [6].

The arrival of the microchip in the 1970s and the subsequent exponential increase in processing power facilitated the development of faster and more powerful systems incorporating digital beam forming, signal enhancement, and new ways of interpreting and displaying data, such as power Doppler. Using a 2 MHz Doppler probe, we can measure blood mean flow velocities of the arteries of the circle of Willis and basal cerebral arteries [7].

So Transcranial Doppler is used for;

1. Detection of intracranial stenosis and occlusion.
2. The course of vasospasm in patients who develop subarachnoid hemorrhage.
3. The detection of cerebral emboli.
4. Prediction of stroke associated with sickle cell disease.
5. Evaluation for brain death [8].

This study evaluated the usefulness of transcranial ultrasound and color Doppler in detecting intracranial lesions and congenital brain anomalies in neonatal age group.

2. Patients and Methods

This study was carried out on 30 patients with suspected intracranial brain lesions, those patients admitted to the neonatal ICU unit at Shibin El Kom Teaching Hospital. The study was done after an approval from institutional ethical committee Banha University. Informed consents were obtained from the neonates guardians.

Patient selection was based on certain Inclusion criteria involve neonates with suspected pathological situations.

There were no significant exclusion criteria, however, some neonates whom were unfit for the examination especially with low oxygen saturation less than 90% due to lack of oxygen source in hands during transportation to radiological department were excluded from the study.

All patient in this study underwent the following:

History taking including: date of birth, gestational age, mode of delivery (spontaneous or Cesarean section), Apgar score at minutes 1, 3 and 5. Need for ventilation support (continuous positive airway pressure or mechanical ventilation), presence of multiple pregnancy, maternal illness, use of drugs during gestation and history of birth insult, Presence of neurological symptoms.

Clinical Examination: General examination stressing on encephalopathy, jaundice and lower limb edema.

Transcranial Ultrasonography and Color Doppler:

Cranial ultrasonography was performed with Linear Array transducer (7.5 MHz).The anterior fontanel was used as the principal acoustic window. Additional windows (mastoid, temporal and posterior fontanel) were used particularly to assess the posterior fossa structures, brain stem and the vascular supply of the brain.

1-The scanning thorough the anterior fontanel included:

A. Five standard coronal planes: Frontal lobes and roof of the orbits, Frontal horns of the lateral ventricles, Foramen of Monro and the third ventricle, Body of the lateral ventricles, Occipital lobes.

B. Five standard sagittal planes: Mid-sagittal plane, Left and right parasagittal planes through lateral ventricles (caudothalamic view), Left and right parasagittal planes through insulae.

2. Additional windows (mastoid window, temporal and posterior fontanel):

For evaluation of posterior fossa structures (cerebellum, 4th ventricle, basal cisterns, occipital lobe, occipital horn of lateral ventricles), Doppler of circle of willis and the vascular supply of the posterior fossa, detection of brain stem lesions.

Transcranial color Doppler: By using a 2 MHz doppler probe and measuring peak systolic, end diastolic, time-averaged velocities and resistive index of the arteries of the circle of Willis including; middle cerebral artery (MCA), anterior cerebral artery (ACA) and posterior cerebral artery (PCA) and also studying the venous supply of the brain.

Statistical methodology

The data collected were tabulated & analyzed by SPSS (Statistical package for the social science software) statistical package version IBM compatible computer.

Quantitative data were expressed as mean and analyzed by comparison of the groups according to the findings.

Qualitative data were expressed as number and percentage (No & %).

3. Results

Patients' demographic data are illustrated in Table (1)

Four main Ultrasound approaches were used; anterior fontanel (AF), [additional winows: (posterior fontanel, mastoid (poster lateral) fontanel, temporal approach]. Table (2)

The examined patients can be classified into 6 main groups as seen in Table (3). A) Normal cases in the study: 11 normal cases are seen in the study. B) Traumatic cases: Traumatic cases related to the study were 1 case by examination showing connatal cyst. C) congenital cases: 3 holoprosencephaly, 2 septo-optic dysplasia,1 cerebellar hypoplasia.

Sonographic findings of the congenital group: For Holoprosencephaly seen as: A lobar type: appear as a single ventricle, Coronal ultrasound scans anteriorly demonstrating the single midline ventricle, Coronal ultrasound scans posteriorly demonstrating the monoventricle becomes enlarged and sac-like. The septum pellucidum is absent. Lobar type: appear by coronal view as absence of septation between two frontal horns of both lateral ventricles and part of the body of them with markedly dilated ventricular system. For septo-optic dysplasia:

appear as Absence of septation between two frontal horns of lateral ventricles and absent crawling sign of anterior cerebral artery under frontal lobe of brain. For cerebellar hypoplasia: decrease size of cerebellum with mega cistern magna and CSF spaces. Table (3)

Table (1) Patients' demographic data

AGE		**No. of patients**
From 1 Day to 3 Days		8(26.7%)
From 4 Days to 14 days		15(50%)
From 15 Days to 29 Days.		7(23.3%)
Gender	Female	17(53.7%)
	Male	13(43.3%)

Table (2) US approaches used in the study.

US Approach	No. of Patients
Anterior fontanel	30
Additional windows	18

Table (3) the number of patients with each type of the neonatal brain insults.

Group	Type of the case	No. of the patients
A	Normal	11
B	Traumatic	1
C	Congenital	6
D	Vascular	10
E	Inflammatory	1
F	Ventriculomegaly	2

In this study 10 cases related to vascular lesions were seen: 3 cases from them are germinal matrix haemorrhage & according to Grades of subependymal haemorrhage, seen as: Grade I =1 case, Grade III = 1 cases and Grade IV = 1 case. 3 cases were periventricular leucomalacia (PVL): 2 Cases as early stage of PVL and 1 case as severe stage of PVL. 1 case as Galen Vein Aneurysm.

Sonographic Findings of Galen Vein Aneurysm are seen as Anechoic cyst Shows high vascularity on Doppler, Multiple

dilated surrounding feeding vessels and Supratentorial Hydrocephalus. Table (3;

Table (5

Table (4) showing the vascular lesions seen in the study.

Diagnosis	No. of cases
Germinal matrix hemorrhage.	3
Periventricular leukomalacia.	3
Brain parenchymal hematoma.	2
Aneurysm of vein of Galen.	1
Extra-axial hemorrhage.	1

Table (5) showing showing hemorrhagic cases seen in the study.

Hemorrhagic	Grade I	Grade II	Grade III	Grade IV
cases seen in the study	1	1	1	1

An example for cases:

35 weeks female preterm neonate, delivered by CS, with no history of maternal illness or birth insult, presented with respiratory distress and fever, no neurological symptoms, examined by CUS in day 29 after delivery.

Examination revealed marked dilatation of the ventricular system with effacement of brain sulci and gyri and shift of midline to left side, also CSF showing internal echoes and thick septations ventriculitis.

Fig. (1): showing marked dilatation of frontal horns of both lateral ventricles(arrow) with effacement of brain sulci and gyri and shift of midline to left side.

Fig. (2) Showing internal echoes (arrow) and thick septations especially in markedly dilated right lateral ventricle so ventriculitis is diagnosed.

4. Discussion

In our study, the examined patients categorized into six groups; eleven cases are normal (group A)**,** one patient is traumatic case (group B)**,** six patients are congenital cases (group C)**,** ten patients are vascular cases (group D)**,** one patient is inflammatory case (group E)**,** one case of ventriculomegaly patient (group F).

These approaches, which include anterior fontanelle imaging, temporal approach imaging, posterior fontanelle imaging, and mastoid fontanelle imaging, aid in detecting pathologic diseases and anatomical anomalies in the infant brain, particularly vascular lesions in circle of wills [9].

In our study, the anterior fontanelle was the first most commonly used. It is of great significance in most of the groups especially group (A), (B) and (C), where it had a great advantage in showing excellent detailed anatomical view of the intracranial structures as well as relatively wide field of view. It is also very helpful in assessing supra-tentorial associations and complications. Examination through the anterior fontanelle is very easy to be performed and to be understood due to the direct coronal and sagittal images obtained which are simulating to a great extent those obtained by other imaging modalities (as CT and MRI) which facilitates correlation of the CUS findings with other modalities.

In concordance with our study, Jačiško et al. [10] discovered that anterior sonography significantly boosts the examiner's confidence while analyzing the infant brain, and that posterior fontanel sonography offered valuable diagnostic information on congenital cystic abnormalities and infections in the posterior fossa.

In our study, temporal approach used mainly for assessing the vessels forming the Circle of Willis in vascular and neoplastic lesions. Otherwise, it wasn't very helpful in assessing the posterior fossa area. In our study, mastoid fontanelle shows a lot better detailed anatomical view of the intracranial structures and a lot wider field of view. Mastoid approach has another disadvantage in that it is a very poor access to the supratentorial and anterior intracranial structures (which must be assessed for common associations and complications) due to the increased distance between the probe and these structures as well as the previously mentioned limited field of view.

This agreed with the study that detected that the posterolateral (mastoid) fontanelle images showed the posterior fossa abnormality better than the anterior fontanelle images did in 23 (96%) of the 24 patients, increased confidence in the diagnosis of 18 (75%) of the 24 patients, and was the only technique to reveal the posterior fossa abnormality in 11 (46%) of the 24 patients [11].

There were attempts to use the foramen magnum but the need of keeping the patient sitting or leaning forwards limited its use as our cases are of the neonatal age group.

In disagreement with our study, Bir et al. [12] reported that the foramen magnum view is a valuable adjunct technique for identifying previously concealed disease and boosting diagnostic confidence.

In our study, group C (congenital malformations) 6 patients, 3 patients had holoprosencephaly (one of them was lobar type and the others were alobar type ,2 patients had septo-optic dysplasia (one of them associated by arachnoid cyst in posterior fossa, the last case had cerebellar hypoplasia.

In our study, main sonographic findings in holoprosencephaly are absent or poor development of the midline structures.

This agreed with the studies of [13, 14] that stated that the diagnosis of holoprosencephaly includes complete or nearly complete lack of separation of the cerebral hemisphere.

In our study at group (D) with Vascular lesions 11 cases, main sonographic findings in vein of Galen malformation are the presence of a highly vascular anechoic cyst at the site of the quadrigeminal cistern with multiple dilated surrounding feeding vessels associated with supratentorial hydrocephalus.

In contrast to our study, Crnogorac et al. [15]stated that vein of Galen malformations are often diagnosed as an anechoic, tubular midline structure superior to the cerebellum. On color Doppler pictures, it exhibits enhanced flow. A tortuous network of dilated arteries is usually visible in the region of the malformation.

Not only has ultrasound supplanted CT as the primary diagnostic tool because to its similar resolution for identifying bleeding, but also because CT has the drawback of needing the unwell preterm newborn to be transferred and exposing the brain and eyes to ionizing radiation [16] .

Importantly, US is cheaper than CT and more accessible to many neonatal intensive care units especially in developing countries [17]

However, CT is useful for identifying complicated hemorrhagic lesions such as subdural hemorrhage, hemorrhagic posterior fossa lesions, and specific cerebral parenchymal hemorrhagic abnormalities [16].

MRI has been demonstrated to produce more accurate pictures of IVH, particularly in the initial few days following the hemorrhage [17].

However, MRI currently cannot supplant ultrasonography in the evaluation IVH, because the former technique requires transport to the scanner, has a relatively long data acquisition time, precludes the use of metallic materials still often found on neonatal monitoring and support equipment, and is expensive [18].

MRI lacks of sensitivity in the detection of hemorrhage in the acute phase [18].

US was found to be an excellent predictor of germinal layer hemorrhage, intraventricular hemorrhage, and hemorrhagic parenchymal infarction on MRI. On early scans, somewhat more germinal layer hemorrhage was considered to be evident on US than on MRI. However, MRI may play a role in determining the full extent of any parenchymal injury once the infant's general condition has stabilized, as demonstrated by a study demonstrating that MRI performed between 29- and 44-weeks postconceptional age is superior to ultrasound and CT in determining the extent of any parenchymal injury and in differentiating parenchymal injury associated with PVH/IVH [18].

In our study Group (D) represents the vascular lesions with 10 cases which includes the hemorrhagic lesions with its grades, Grade I we found 3cases, Grade I one case, Grade III we found 1 case and Grade IV also 1 case, which is matching with other studies, The subependymal germinal matrix is the predominant location of bleeding in IVH. The germinal matrix is the tissue in which neurons and glial cells form prior to migrating from the subependymal area to the cortex [19].

The germinal matrix is densely packed with cells, lacks connective supporting tissue, and is densely vascularized with extremely fine capillaries. The increased capillary fragility may explain the high frequency of these hemorrhages in preterm infants. Furthermore, the germinal matrix has a high fibrinolytic activity that may be important for the extension of the capillary Hemorrhages the originate in this tissue [19]. By 34 to 36 weeks of gestation, the germinal matrix has involuted; cells from this zone have nearly completely migrated by 40 weeks. The final portion of the germinal matrix to involute is the region surrounding the caudate head (caudo-thalamic groove), which is the most prone to bleeding due to its prolonged metabolic activity [20].

Periventricular- Intraventricular hemorrhage is graded by us scan as follows:

- **Grade I** isolated germinal matrix hemorrhage with no intraventricular extension.
- **Grade II**—germinal matrix hemorrhage with extension into the ventricular system but without any ventricular dilatation.
- **Grade III**—IVH with ventricular dilatation.
- **Grade IV**—characterized by intraparenchymal haemorrhage (**Papile LA., 1978**, **Acarregui, 2008),** Grades I and II are also referred to as minor IVHs, whereas grades III and IV are considered major IVHs.

Spaide et al. and Saxena et al. [21’22]stated that Doppler flow measurements may aid in the differentiation of vascular structures from non-vascular lesions and that CCD can be used to research cerebral hemodynamics by monitoring the primary intracranial arteries and big veins.

In our study, also CCD and TCD were very beneficial in detecting vascularity of the lesions and assessment of the intracranial vessels which is deficit in other modalities as CT and MRI; for example, it was used to study the avascular nature of cystic lesions, hematoma and extra-axial lesions, to detect any associated vascular anomalies with the congenital brain abnormalities

CUS examination needs operator experience, proper instrument control settings and at least one accessible window in different groups. The examination is also degraded by patient movement.

This agreed with which stated that limitations of CUS include that image quality can be affected by small acoustic windows, some lesions resulting from infection such as micro abscesses, encephalitis may not be optimally recognized by CUS [23] and myelination is not visualized.

CUS has proven to be an important diagnostic tool in evaluating the neonatal brain insults. Being fast, easy, available and safe it has a great role in diagnosis of the brain abnormality, detection of common complications and associations as well as for follow up.

Regarding the technique, the CUS examination should be done through all available acoustic windows (if accessible) including the anterior fontanelle, posterior fontanelle, mastoid and temporal approaches, foramen magnum as well as any skull defect (if present).

Regarding the congenital malformations, efficient CUS can be diagnostic in most of the cases with no need for other additional imaging modalities. It also aids in detecting associated abnormalities eg. corpus callosum agenesis or complications eg. hydrocephalus.

5. Conclusions

In conclusion, US has been a major advance in the study of neonatal brain, it is portable safe, non-invasive, low cost and highly effective technique that is of considerable value in evaluation of neonatal intracranial disorders and should be included within integrated approach to CNS imaging in the neonates.

Financial support and sponsorship: Nil
Conflict of Interest: Nil

References

[1] G.Orman, J.Benson, C.Kweldam, T.Bosemani, A.Tekes, M.Jong. VIEWS AND REVIEWS Neonatal Head Ultrasonography Today: A Powerful Imaging Tool.vol.15,pp.144-150,2014.

[2] SY.Ng, AYW.Lee Traumatic Brain Injuries Pathophysiology and Potential Therapeutic

Targets. Front Cell Neurosci.vol.13,pp.170-180,2019.
[3] SA.Back White matter injury in the preterm infant: pathology and mechanisms. Acta Neuropathol.vol.134,pp.331-49,2017.
[4] XB.Liu, Y.Shen, JM.Plane, W.Deng Vulnerability of premyelinating oligodendrocytes to white-matter damage in neonatal brain injury. Neurosci Bull.vol.29,pp.229-38,2013.
[5] A.Parodi, P.Govaert, S.Horsch, MC.Bravo, LA.Ramenghi Cranial ultrasound findings in preterm germinal matrix haemorrhage, sequelae and outcome. Pediatr Res.vol.87,pp.13-24,2020.
[6] AA.Oglat, MZ.Matjafri, N.Suardi, MA.Oqlat, MA.Abdelrahman, AA.Oqlat, A Review of Medical Doppler Ultrasonography of Blood Flow in General and Especially in Common Carotid Artery. J Med Ultrasound.vol.26,pp.3-13,2018.
[7] S.Badiger, PT.Akkasaligar, Medical Imaging Techniques in Clinical Medicine. World Academy of Science, Engineering and Technology, International Journal of Medical, Health, Biomedical, Bioengineering and Pharmaceutical Engineering.vol.8,pp.812-7,2014.
[8] S.Rawal, C.Barnett, A.John-Baptiste, HH.Thein, T.Krings, GJ.Rinkel, Effectiveness of diagnostic strategies in suspected delayed cerebral ischemia: a decision analysis. Stroke.vol.46,pp.77-83, 2015.
[9] P.Gupta, KS.Sodhi, AK.Saxena, N.Khandelwal, P.Singhi, Neonatal cranial sonography: A concise review for clinicians. J Pediatr Neurosci.vol.11,pp.7-13,2016.
[10] J.Jačiško, K.Mezian, O.Naňka, Sonography of the anterior cruciate ligament revisited. J Clin Ultrasound.vol.49,pp.248-9,2021.
[11] M.Soudack, J.Jacobson, L.Raviv-Zilka, A.Ben-Shlush, J.Kuint, Cerebellar hemorrhage in very low birth weight premature infants: the advantage of the posterolateral fontanelle view. J Clin Ultrasound.vol.41,pp.395-401,2013.
[12] SC.Bir, TK.Maiti, A.Nanda, Foramen magnum meningiomas. Handb Clin Neurol.vol.170,pp.167-74,2020.
[13] EF.Kauvar, M.Muenke, Holoprosencephaly: recommendations for diagnosis and management. Curr Opin Pediatr.vol.22,pp.687-95,2010.
[14] TC.Winter, AM.Kennedy, PJ.Woodward, Holoprosencephaly: A Survey of the Entity, with Embryology and Fetal Imaging. RadioGraphics.vol.35,pp.275-90,2015.
[15] S.Crnogorac, Bozaric AV. Galen Vein Aneurysm- Challenge for Treatment. Open Med (Wars) .vol.12,pp.440-5,2017.
[16] Argyropoulou MI, Veyrac C. The rationale for routine cerebral ultrasound in premature infants. Pediatr Radiol. 2015;45:646-50.
[17] IGS.Cheah, Economic assessment of neonatal intensive care. Transl Pediatr.vol.8,pp.246-56,2019.
[18] B.Putbrese, A.Kennedy, Findings and differential diagnosis of fetal intracranial haemorrhage and fetal ischaemic brain injury: what is the role of fetal MRI? Br J Radiol.vol.90,pp.201-6253,2017.
[19] L.Zhao, Y.Jiang, Y.Wang, Y.Bai, Y.Sun, Y.Li, Spinal Epidural Cavernous Hemangiomas: A Clinical Series of 9 Cases and Literature Review. Frontiers in Oncology,pp.11,2021.
[20] P.Ballabh, Intraventricular hemorrhage in premature infants: mechanism of disease. Pediatr Res.vol.67,pp.1-8,2010.
[21] Spaide RF, Fujimoto JG, Waheed NK, Sadda SR, Staurenghi G. Optical coherence tomography angiography. Prog Retin Eye Res. 2018;64:1-55.
[22] A.Saxena, EYK.Ng, ST.Lim, Imaging modalities to diagnose carotid artery stenosis: progress and prospect. Biomed Eng Online.vol.18,pp.66,2019.
[23] SJ.Steggerda, G.van Wezel-Meijler, Cranial ultrasonography of the immature cerebellum: Role and limitations. Semin Fetal Neonatal Med.vol.21,pp.295-304,2016.