Review Article

TRANSCRANIAL REAL TIME UNTRASONOGRAPHY— A DISGNOSTIC TOOL IN NEONATAL INTRACRANIAL HEMORRHAGE

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Intracranial hemorrhage (ICH) is a major cause of morbidity and mortality in neonates especially those less than 32 weeks of gestation(1-3). The reported incidence of ICH in high risk preterm neonates varies between 40-50%(3,4). Previously the diagnosis of ICH was made by computerized tomography (CT) of the head(4-6). Although studies using computerized tomography have been highly informative, the technique has serious limitations. A very ill infant may require sedation for optimal studies; the infant must be transported to the Radiology Department which may not be desirable for an acutely sick neonate with ICH; and the hazards associated with ionizing radiations are of major concern(5-8). B-mode, gray scale, and real time ultrasound provide another method for examining the brain(5,9-15).

Real time ultrasound (RTU) was first used in a neonatal intensive care unit (NICU) to detect intraventricular hemorrhage (IVH) in the year 1978(9), and gradually it has been adopted by many NICUs for this purpose(5,11,12,16,17). The procedure has a high sensitivity (96%) and specificity (94%) in diagnosing ICH other than subarachnoid hemorrhage compared with CT(17). The portability of the RTU units, abscence of hazards associated with ionizing radiations, recent availability of high frequency transducers (>5 MHz), and ability to perform scanning quickly (<5 min) with the patients inside the incubators makes ultrasound an ideal modality for detection of ICH in neonates.

Despite being established as a sensitive and non-invasive method of detecting IVH and for detection of intraparenchymal extension of hemorrhages and post-hemorrhagic ventriculomegaly (PHV), only few NICUs all over the world have the facility of round the clock RTU scanning(18). The purpose of this communication is to further highlight the need for an RTU scanner in any NICU catering sick premature babies.

Technique and Normal Sonographic Appearances of Neonatal Cerebral Ventricles

A real time ultrasound unit (RTU) with 90° field of vision and internally focussed transducers of 5 and 7.5 MHz is most appropriate for sonography of cerebral ventricles(5,11,16,17). The examination is done in three planes, *i.e.*, coronal and, right and left angled-sagittal (parasagittal) views. No sedation is required.

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To study the coronal plane, the transducer is placed over the anterior fontanelle following the coronal suture and rocked slightly backward and forward. By angling the transducer towards the back of the head, the posterior regions of the brain can be examined. The opposite angulation allows visualization of the frontal regions of the brain. Coronal section at head of the caudate nucleus demonstrates both lateral ventricles (slit like), thalmi and caudate nuclie (*Fig. 1*). By turning the transducer 90° upon itself from the coronal plane, right and left angled-sagittal views can be obtained.

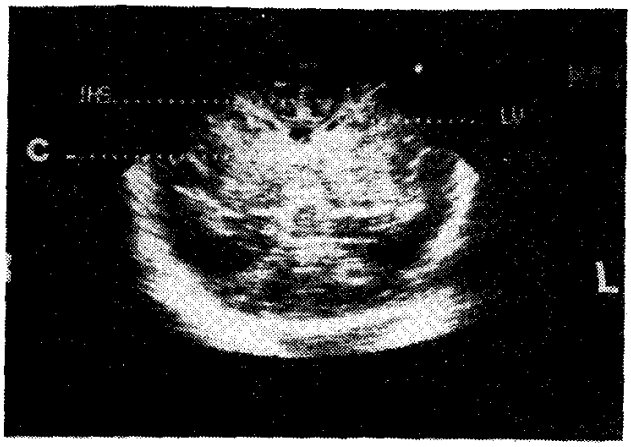

Fig. 1. Coronal sonogram at level of head of the caudate nucleus showing normal lateral (LV) and cavum septum pollucidum (c).

Para-sagittal sections (right and left) are the most important views since they often reveal most of the desired information. This section (*Fig. 2*) demonstrates anechoic lateral ventricle of the corresponding side (frontal horn, body, atrium, and occipital horn), choroid plexus, thalmus and caudate nucleus. The roof of the lateral ventricle is formed by corpus callosum.

The sagittal studies are essential to identify choroid plexus which is a highly echo-dense structure surrounding the hypoechoic thalmus. It normally pulsates with heart beat, which facilitates its identification with RTU. At the body of the lateral ventricle, the plexus lies over the thalmus and is 2-3 mm high. The boundary between the echo-dense choroid plexus and the hypo-echoic thalmus is the landmark with which to identify floor of the lateral ventricle. At the ventricular atrium the plexus lies posterior to the thalmus. It can extend up to 15 mm in the sagittal plane with a classical normal superio-anterior tapering but does not occupy the atrium completely.

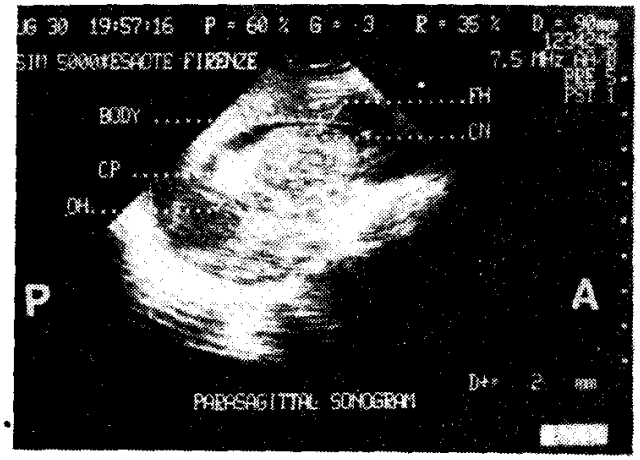

Fig. 2. Para-sagittal sonogram showing normally echo-free lateral ventricle (frontal horn, FH; body; occipital horn, OH), echo-dense choroid-plexus (CP) and hypoechoic thalmus (TH).

In the sagittal plane the occipital horn of the lateral ventricle appears as an anechoic triangle posterior to the thalmus and the choroid plexus (*Fig. 2*).

Sonographic Appearances of Intracranial Hemorrhages in Neonates

The real time sonographic evaluation of intracranial contents is a rapid and accurate method of diagnosing ICH in newborns(3,11,16,17,19,20). In preterm

neonates, four grades (I-IV) of ICH can be identified sonographically(5).

Grade I hemorrhage is isolated to germinal matrix and is termed as subependymal hemorrhage (SEH). SEH typically appears sonographically as an echodense focus in the area of caudate nucleus/caudo-thalmic notch (*Figs. 3, 4*). It appears on the inferolateral aspect of the lateral ventricle as a highly echodense region with convex borders. It may be unilateral but is frequently bilateral and symmetric. SEH in the germinal matrix is the commonest type of ICH in pre-terms.

The germinal matrix is composed of cells that develop into neurons and glia of the cerebral cortex and basal ganglia. These cells are loosely organized, contain a rich vascular supply and form the entire surface of the lateral ventricle till approximately 12-14 weeks gestation. By six months gestation age the germinal matrix is present only along the ventricular surface of the head and part of the body of the caudate nucleus and thalmus and hence SEH occurs in this area. The germinal matrix cells have migrated out completely by term in most cases, and thus SEH is uncommon as the brain matures.

Grade II hemorrhage is extension of SEH into the normal sized ventricles (*Figs. 4-5*). Recent IVH is echo-dense. Small IVH is most difficult to diagnose since small clots may adhere to the rough surface of choroid plexus or may be found in the occipital horn or ventricular atrium. Since the choroid plexus and IVH are isoechoic, adherent clot is implied by identifying the contour abnormalities of the choroid-plexus echo-complex. Extension of the choroid-plexus echo-complex into the occipital horn, irregularities of its surface, or loss of normal superio-anterior tapering, or loss of its pulsations are all relatively subjective signs that suggest adherent hematoma.

Grade III hemorrhage is IVH with ventricular dilatation. Large hemorrhages fill and expand the ventricles, and the hematoma is well defined and appears like a ventricular cast (*Fig. 6*).

Grade IV hemorrhage may be the intra-parenchymal extension of the SEH (*Fig. 7*), or intra-parenchymal hemorrhage alone(21). ICH is most commonly seen in preterm neonates, especially those <32 weeks of gestation(1-3). The reported incidence of ICH as detected by real time ultrasonography in preterm neonates <32 weeks of gestation varies between 26-90%(3,12,16,17). Pre-term neonates with pulmonary complications are also at a greater risk for ICH(22).

In a recent prospective study (unpublished data), we carried out real time sector cranial sonography with a 7.5 MHz internally focussed transducar on 70 preterm neonates (gestational age <34 weeks) and 30 full-term neonates with severe birth asphyxia (SBA) for any evidence of ICH. All the scans were performed by one of the authors (AKG), especially experienced for neonatal neurosonography. Examinations were performed within first 24 h of birth and then at 48, 72, 96 and 120 hours and thereafter at weekly intervals until discharge or death. The overall incidence of ICH was 22% (n=22). All hemorrhages occurred within 96 hours of life; 50% being diagnosed with the first scan. Preterm neonates had a significantly higher incidence of ICH (28.6%) as compared with term infants with SBA (6.66%). The infants especially at risk were those less than 32 weeks' gestation (odds ratio, 29) and/or birth weight less than 1200 g (odds ratio, 6).

Table I shows the clinical presentation, distribution of ICHs by grades, and imme-

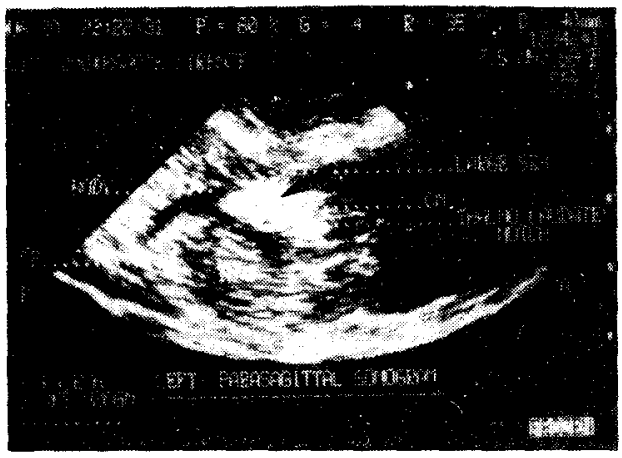

Fig.3. Para-sagittal sonogram (left) showing subependymal hemorrhage (arrow) in the region of caudate nucleus (CN).

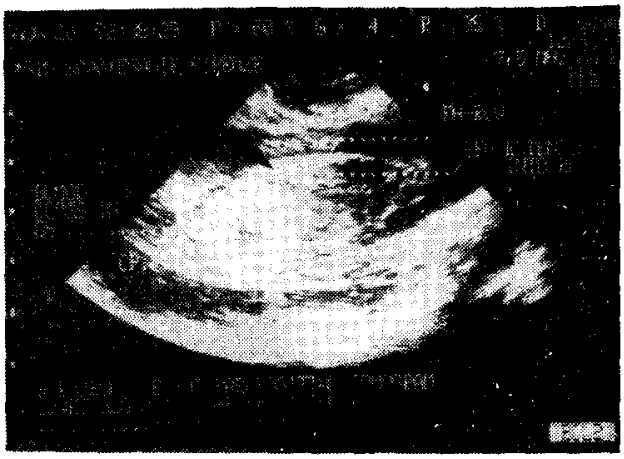

Fig.5. Para-sagittal scan (right) showing SEH extending into normally sized lateral vetrical-Grade II IVH (arrow).

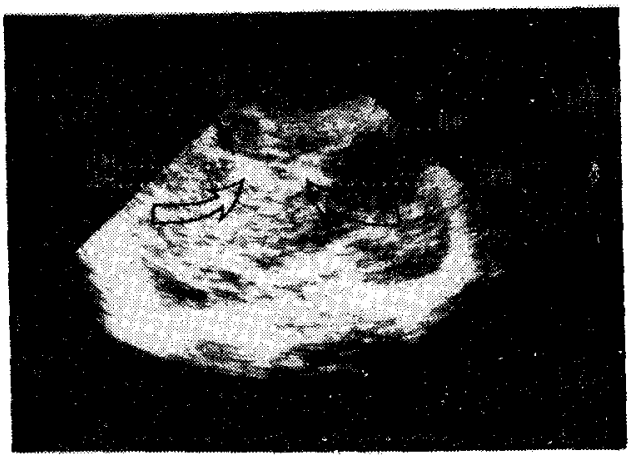

Fig.4. Coronal scan showing bilateral Grade I hemorrhage (open arrows) with extension into the normally sized right lateral ventricle-Grade II IVH (arrow).

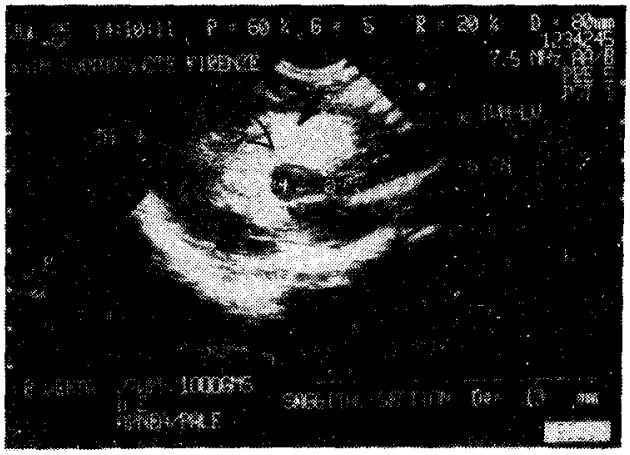

Fig. 6. Para-sagittal sonogram (Rt) showing severe intraventricular hemorrhage (open arrow) surrounding the hypoechoic thalmus (TH) with extension into cortex (arrow).

diate outcome of these neonates. Larger grades of hemorrhages were generally symptomatic while a majority of patients with small hemorrhages had no associated symptoms. Two major clinical syndromes were associated with SEH-IVH: (*i*) catastrophic deterioration; and (*ii*) a more saltatory deterioration. The first was the classic presentation of a major hemorrhage, *i.e.,* a catastrophic neurologic deterioration that usually evolved in minutes to hours and consisted of deep stupor or coma, respiratory abnormalities, seizures, non-reactive pupils, flaccid quadriparesis, often accompanied by falling hemotocrit, bulging anterior fontanelle, systemic hypotension, hypothermia and bradycardia(23). On the contrary, saltatory syndrome tended to evolve over hours to days, often slowly, and was characterized by change in level of alertness, a decrease in spontaneous and elicited movements, hypotonia and subtle

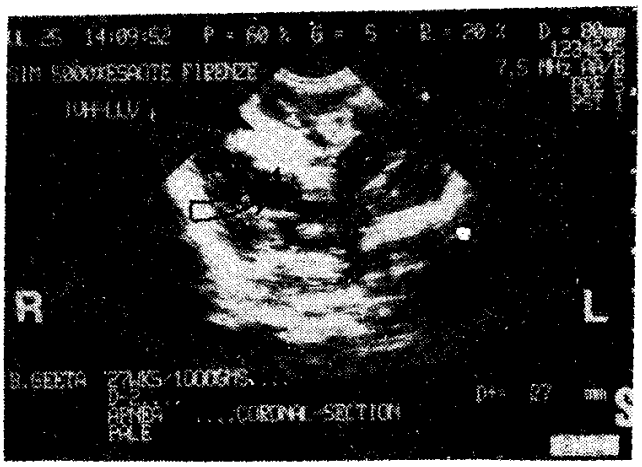

Fig 7. Coronal sonogram showing right sided IVH (open-arrow) with extension into the cortex (Grade IV) (arrow).

abnormalities of eye position(23).

Overall immediate mortality was 12%, and correlated to severity of hemorrhage, being greatest in Grade III/IV-IVH. Two of the four neonates who survived Grade II IVH subsequently developed post-hemorrhage ventriculomegaly at 7 and 10 days of age, respectively. On follow-up, ventriculomegaly disappeared in one and got arrested in the other neonate at the age of 4 weeks. The lone survivor of Grade III IVH developed progressive ventriculomegaly immediately after the diagnosis of hemorrhage and expired at the age of three weeks despite serial lumbar punctures. One of the survivors with SEH developed features suggestive of cystic periventricular leucomalacia at the age of four weeks.

Sonographic Evaluation of Complications of ICH

Small SEHs usually resolve completely over a period of several weeks. Large Grade I hemorrhages, however, often leave behind a sub-ependymal cyst(17).

Resolution of Grade II/III IVHs follows a specific pattern. Sequential sonograms reveal that the originally homo-

TABLE I—*Distribution of 22 Cases of ICH by Grades*

Grade of hemorrhage	No. of patients	Presentation (C/F)	Immediate outcome	
			Survived	Died
I	8	Asymptomatic–8 Symptoomatic–0	5	3*
II	8	Asymptomatic–1 Symptomatic–7 (ST-5, CT-2)	4	4
III	4	Asymptomatic-0 Symptomatic–4 (ST-1, CT-3)	1	3
IV	2	Asymptomatic-0 Symptomatic–2 (ST-0, CT-2)	0	2

ST = Saltatory presentation, CT = Catastrophic presentation.
* Died of hyaline membrane disease.

TABLE II–*Sonographic follow-up of Neonates Surviving Initial Episode of ICH (n = 10)*

Grade of hemorrhage	No. of patients	Results of weekly follow-up-sonography for 2 wks after initial diagnosis			Outcome	
		Normal	PHV	Decreased	Discharged	Died
I	5	2	0	3*	2**	0
II	4	0	2	2*	2	2+
III	1	0	1	0	0	1+
IV	0	0	0	0	0	0

+ PHH; * Still under follow-up; ** Developed PVL.

geneous clot undergoes central liquefaction; resulting in anechoic areas interspersed with echo-dense blood clots. Over a period of as much as 8 weeks, the intraventricular clots gradually decrease in size and eventually disappear(17).

After Grade II/III hemorrhages, however, development of post hemorrhagic hydrocephalus (PHH) is of great concern(11,16,17). For its early diagnosis, neonates with Grade II/III hemorrhages should be evaluated by weekly cranial sonograms. The size of the initial hemorrhage correlates reasonably well with the severity of PHH; after large IVHs fairly severe post-hemorrhagic ventriculomegaly (PHV) can develop. In a recent prospective study, we detected PHV in 50 and 100% survivors of Grades II and III-ICH, respectively (*Table II*). Most commonly, PHV is a self limiting process. Sequential sonograms done by previous workers suggest that most patients undergo a period of initial ventricular enlargement followed by stabilization and eventual recovery to normal or near normal. However, some neonates with PHV may have an intractable hydrocehalus necessitating repeated CSF withdrawal or even shunt surgery. All the babies with PHV under our follow up, however, expired before any intervention cound be done.

As is seen with other forms of ICHs, parenchymal extension of SEH, *i.e.,* Grade IV hemorrhage too shows a specific pattern of resolution. Initially, the hematoma is uniformally echogenic. The central portion of the clot gradually becomes hypoechoic and eventually the clot retracts leaving behind a discrete porenchephalic cyst(11,16,17).

Periventriclar leucomalacia, *i.e.,* symmetric bands of increased echogenicity around the lateral ventricles may also be seen in some preterm infants who have had IVH and or birth asphyxia in the neonatal period. It has been suggested that release of vasoactive substances from IVH may produce local ischemia which ultimately results in PVL(24).

Sonographically PVL classically appears as bilateral symmetric areas of periventricular increased echogenicity with in homogeneous internal echotexture and irregular borders unlike hemorrhage.

Further, inter-hemispheric fissure may be widened but typical cystic lesions takes as much as 4-6 weeks to appear(24).

Limitations and Prognostic Implications of Neonatal Cranial Sonography in the Diagnosis of ICH

Real time ultrasound of the neonatal brain has been widely adopted in the West because the manufacturers of ultrasound units have developed machines that produce, by means of sound, an image which appear to resemble the structure of the brain. We interpret echoes by reference to the anatomical slices produced by pathologists and believe that the image gives us the same information.

Several studies are now available that report the accuracy of sonography in the diagnosis of SEH-IVH(5,16,17), but the correlation of appearances with other conditions is unfortunately limited and may be misleading. We now know that extensive echogenicity within the brain may be associated with a macroscopically normal brain at necropsy(10) and, conversely, pathological features within or around the brain such as epidural or subdural hematomas and subarachnoid hemorrhage may not be detected by RTU(16-18). Further, very small IVHs are also likely to be missed on sonography if the ventricular size is normal(16,17).

Reliable prognostic information about ICH is just becoming available but still there is considerable confusion in this area. SEH (Grade I) hemorrhage was initially thought to be associated with an adverse neurological outcome of some infants(18). It was only some time later when it was realized that Grade I hemorrhage confined to the germinal layer matrix was a benign condition(5,25,26). However, more recent studies have questioned the benign nature of SEH(27). Grades II-IV appearances of IVHs on sonography, however, have a high sensitivity (66%) and specificity (96%) of predicting later development of cerebral palsy(27).

There is now enough evidence that cystic brain lesions, *i.e.,* PVL and porencehalic cysts are the most sinister lesion in terms of long term neurological prognosis and variables such as size, extent, and position of the cavities are important in more accurately predicting both cerebral palsy and developmental delay(27).

In conclusion accurate assessment of neonatal brain anatomy and pathology can now be obtained with commercially available real time ultrasound equipments. If available, good quality real time, transfontanelle sector scanning should include all premature neonates of gestational age <32 weeks. Initial examinations should be carried out daily in first 4 days of life and/or at any time when there is a clinical suspicion of ICH in any baby. Follow-up examinations after confirming ICH, however, should be done weekly in order to detect post-hemorrhagic complications. Further, a predischarge examination is desirable in all high risk infants in order to detect cystic brain lesions (PVL, porencephalic cysts) which have important long term prognostic implications.

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NOTES AND NEWS

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