

**ULTRASONOGRAPHY OF
THE BRAIN IN PRETERM
INFANTS AND ITS
CORRELATION WITH
NEURODEVELOPMENTAL
OUTCOME**

**S. Chaudhari
A.S. Kinare
R. Kumar
A.N. Pandit
M. Deshpande**

ABSTRACT

Two hundred and eighteen preterm neonates had ultrasonography (USG) brain done on third, and/or seventh and fourteenth day of life. Fifty eight (26.3%) had intraventricular/periventricular hemorrhage, 3 had parenchymal lesions. 46 had Grade I hemorrhage, 9 had Grade II, 2 had Grade III and 1 had Grade IV hemorrhage. Grades III and IV hemorrhages occurred in neonates below 34 weeks gestation. There was an inverse relationship between gestational age and hemorrhage ($p=0.0001$). A comparison of incidence of hemorrhage between preterms who were appropriate for gestational age and those who were small for gestational age was not significant. Out of the 63 neonates who had serial USGs on the third and seventh day of life, 15 of the 16 bleeds (94%) were detected on the third day itself, indicating it to be an opportune time for doing an USG.

USG at term (40 weeks postconceptual age) was done in 99 infants to see if it could correctly predict the neurodevelopmental outcome using the Bayley Scales of Infant Development. Out of

The introduction of cranial ultrasonography (USG) as a regular diagnostic investigation has resulted in increased awareness of the frequency of intracranial lesions in the preterm infant. Periventricular and intraventricular hemorrhage and cerebral ischemia are important causes of mortality and short term and long term morbidity in the preterm infant. The present study was undertaken to detect such intracranial lesions by performing ultrasonography (USG) in the preterm neonates. Several, earlier studies, have correlated the ultra-sonographic findings with mortality and morbidity (1-4).

It is a common practice in the devel-

these 99 infants, 72 came for the developmental assessment at one year. One neonate who had periventricular leucomalacia with cystic changes on USG at term, was grossly abnormal with cerebral palsy and mental retardation. Six infants showed delayed development with a mean mental development quotient of 79.1 ± 1.72 at 2 years. The specificity of USG at term for predicting outcome was 89.2% and negative predictive value was 90%, indicating that a normal USG at term predicted a good neurodevelopmental outcome.

Keywords: Preterm infant, Ultrasonography brain, Neurodevelopmental outcome.

From the Division of Neonatology, Department of Pediatrics, K.E.M. Hospital, Pune 411 011.

Reprint requests: Dr. Sudha Chaudhari, Consultant, Division of Neonatology, Department of Pediatrics, K.E.M. Hospital, Pune 411 011.

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oped countries to do serial USG examinations during the hospital stay(5). However, it is difficult for us to do so due to financial constraints and non-availability of portable USG machines. Ninety per cent of hemorrhages occur before the fourth day of life and 20-30% of these may show progression till the seventh day(6) and ventriculomegaly may develop by the fourteenth day. Hence we decided to do serial USGs on the third, seventh and fourteenth day of life, whenever possible. USG findings at term (40 weeks postconceptual age) have been used as a prognostic indicator of neurodevelopmental outcome(7,8). In the present study, all the babies who had an USG at term were prospectively followed up for a period of one year to determine their neurodevelopmental outcome and to see if any correlation could be established between USG at term and neurodevelopmental outcome.

Material and Methods

The study was done at the Level II Care Neonatal Unit of the KEM Hospital, Pune, during an eighteen month period, from January 1991 to July 1992. The study subjects were preterm neonates with gestational age less than 37 weeks.

Clinical information such as antenatal history, type of delivery, resuscitative efforts, was recorded. Birth weight was measured on an electronic digital scale to the nearest 5 g. Gestational age assessment was done within first 24 hours and reconfirmed at 72 hours, using the modified Dubowitz score(9). The babies were classified as appropriate for gestational age (AGA)

or small for gestational age (SGA) using intrauterine growth curves(10). The clinical course of the neonate was monitored by daily clinical examination and problems such as respiratory distress, seizures, apnea, *etc.*, were recorded. None of these babies were ventilated.

Cranial ultrasound examinations were done through the anterior fontanelle by using an Aloka 280 SSD or 650 machine with a 5MHZ sector transducer in the coronal and sagittal planes. Grading of hemorrhage was done according to the grading system described by Papile *et al.*(11). Three serial USGs were done on 3rd, 7th and 14th day of life, when-ever possible. Only those babies, who had at least one USG according to this protocol were included in this study. After discharge, another USG was advised at term (40 weeks post conceptual age").

All the babies were followed up in a special High Risk Clinic. After discharge, they were called every week in the first month, fortnightly in the second month and subsequently every month till the age of one year. Apart from a routine clinical examination, anthropometric measurements were taken, a neurological examination was done and advice given regarding nutrition and immunization. A detailed assessment of neurodevelopment was done using Baroda norms(12), the Indian adaptation of the Bayley Scales of Infant Development (BSID) at 1 year \pm 15 days. This assessment was done by a trained psychologist in a specially designed sound proof room with a one way vision mirror. Corrected age was used for this assessment. Only those babies who had an USG at term

were prospectively followed up for their neurodevelopmental outcome in this study.

A mental and motor quotient of >84 was considered as normal, 70-84 as delay and below 70 as retardation. Infants were called for the BSID assessment by sending them letters. Those children who had a mental or motor quotient less than 84 at 1 year were called for a second assessment at 2 years.

Results

Two hundred and eighteen neonates with gestation less than 37 weeks (78 in-born, 140 outborn) had USG examination of the brain done during their stay in the neonatal unit. Out of these 218 neonates, 58 (26.5%) had intraventricular/periventricular hemorrhage (IVH/PVH). Forty six neonates had Grade I bleed, 9 had Grade II bleed, 2 had Grade III and 1 had Grade IV bleed. Three neonates had other parenchymal lesions. One had pronounced periventricular flare and two had periventricular leucomalacia (PVL), seen on the seventh

day. The distribution of these neonates according to their birth weight is shown in *Table I*. The major number of hemorrhages occurred in neonates with birth weight less than 1.8 kg. The distribution of hemorrhage according to gestational age is shown in *Table II*. The severe forms of hemorrhage (Grades III and IV) occurred in neonates with gestation less than 32 weeks. There was an inverse relationship between gestational age and hemorrhage (Chi square for linear trend $p = 0.0001$). Out of the 218 preterm neonates, 89 (40.8%) were SGA. The incidence of hemorrhage in AGA neonates was 29.4% and SGA neonates was 22.7%. However, this difference was not statistically significant.

Serial USGs were done whenever possible. In all, 218 preterm infants had 313 USG examinations performed during their hospital stay. However, a large number of babies had a single USG on the third day. Out of the 143 babies who had only one USG on the third day, 39 showed a hemorrhage (*Table III*). USG on the third and seventh day was done

TABLE I—Distribution of USG Findings According to Birth Weight

Birthweight (kg)	Total (n=218)	Positive findings (n=61)	%	Grades of bleed				Parenchymal lesions (n=3)
				I (n=46)	II (n=9)	III (n=2)	IV (n=1)	
<1.0	12	10	83.3	8	1	1	0	0
1.0-1.2	28	19	67.8	15	2	1	1	0
1.2-1.4	49	14	28.7	11	2	0	0	1
1.4-1.6	55	8	14.5	5	2	0	0	1
1.6-1.8	38	7	17.0	5	2	0	0	0
1.8-2.0	25	2	8.0	1	0	0	0	1
>2.0	11	1	9.0	1	0	0	0	0

in 43 babies and three serial USGs on the third, seventh and fourteenth day in 20 babies. Out of these 63 babies who had USGs on the third and seventh day, 15 showed a bleed on the third day and only one additional bleed was detected on the seventh day. Thus 15 out of 16 hemorrhages (94%), were detected on the third day in this group.

It becomes apparent from *Table III* that no new hemorrhages were detected on the 14th day in the 32 babies who had USGs on the seventh and fourteenth day. Additional findings were recorded in 3 other babies. One baby had pronounced periventricular flare and two had periventricular leucomalacia

(PVL) noted on the seventh day. One baby developed ventriculomegaly following a Grade II hemorrhage.

Ninety nine infants had USGs done at term. Sixty six neonates who had normal USGs in the NICU, continued to have normal USGs at term. Twenty one neonates with Grade I bleed showed a complete resolution, 4 remained the same and 3 showed a small subependymal cyst (*Table IV*). The two neonates with Grade II hemorrhage showed complete resolution. One neonate with Grade II hemorrhage who showed ventriculomegaly died with gastroenteritis after going home. One neonate with periventricular leucomalacia (PVL)

TABLE II-Distribution of USG Findings According to Gestational Age

Gestational age (weeks)	Total (n=218)	Positive findings (n=61)	%	Grades of bleed				Parenchymal lesions (n=3)
				I (n=46)	II (n=9)	III (n=2)	IV (n=1)	
<28	18	11	61.1	18	3	0	0	0
29-30	30	17	56.6	14	2	1	0	0
31-32	75	24	32.0	18	2	1	1	2
33-34	59	7	11.8	5	2	0	0	0
35-36	38	2	5.2	1	0	0	0	1

TABLE III-Hemorrhages Detected on Serial USGs

Day of life when use done	Total (n)	Day when hemorrhage was first detected		
		3 (n)	7 (n)	14 (n)
Day 3	143	39	-	-
Days 3 & 7	43	11	1	-
Days 3,7 & 14	20	4	0	0
Days 7 & 14	12	-	3	0

showed progression with cystic changes.

Only infants who had an USG at term were asked to come for a developmental assessment at one year (corrected age). Seventy two of these infants were assessed at one year. A normal motor and mental quotient (>84) was seen in 62 infants. These infants were not followed up any further. One infant who had PVL with cystic changes (Fig. 1) at the term USG was grossly abnormal with developmental quotients below 50. This child was diagnosed as having mental retardation with cerebral palsy. The remaining 9 infants who showed delayed development (70-84) were followed up for a further period of 1 year to see if there was "catch up." All of them caught up in their motor development (MoQ >84) when assessed at 2 years. However, 6 infants still showed a

delay in their mental development with a mean mental quotient of 79.1 ± 1.72 . The correlation between USG findings at term and neurodevelopmental outcome was determined to see if this could be a good predictor of neurodevelopmental outcome. The sensitivity was 14.28% and the specificity was 89.2%. The positive predictive value of the test was 12.5% while the negative predictive value was 90.6%.

Discussion

Two hundred and eighteen neonates with gestation ranging from 27-36 weeks and birth weights ranging from 705-2100 g were examined by a cranial USG. Twenty seven per cent of these neonates showed evidence of IVH/PVH. Other studies report a much higher incidence(13,14). This may be due to the fact that we had a very small num-

TABLE IV-*Correlation of USG Findings with Neurodevelopmental Outcome (BSID) in 72 Infants*

use (in NICU)	use (at term)	n	Development	
			Normal	Delayed
1. Normal	Normal	43	39	4
2. Grade I bleed	Normal	17	15	2
	Unchanged	4	4	-
	Subependymal cyst	3	3	-
3. Grade II bleed	Normal	2	2	-
4. Periventricular flare	Normal	1	1	-
5. Periventricular leucomalacia	Normal	1	1	-
Periventricular leucomalacia	Cystic changes	1	-	1 (grossly abnormal)

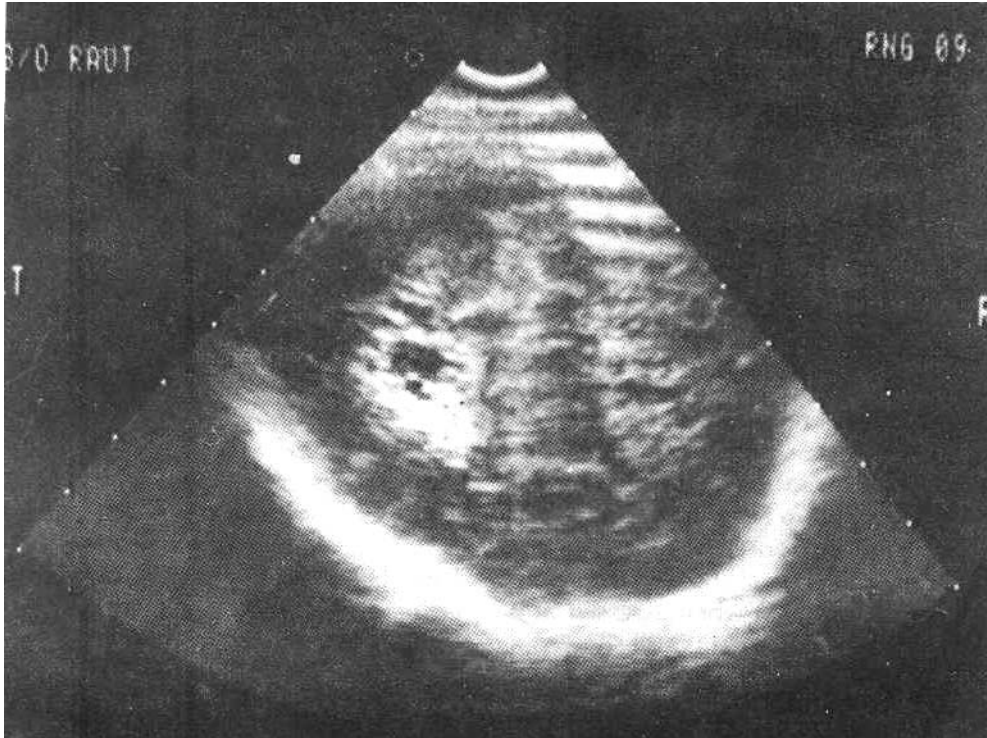


Fig. 1. USF at term showing PVL with cystic changes in a neonate who developed cerebral palsy with mental retardation.

ber of neonates with gestational age <28 wks. The non-availability of a portable USG machine, the lack of ventilatory support and the fact that the first USG was done on the third day, may have contributed to this small number. The incidence of PVH/IVH was much higher (39%) in our previous study(15) because we had selectively examined only those neonates who were at high risk for developing an intracranial bleed.

The incidence of IVH/PVH was higher in neonates with a birth weight

less than 1.4 kg. Since 40% of neonates in our study were SG A, the incidence of bleeds in SGA and AGA babies was compared. However, this difference was not statistically significant. Procianoy(16) has shown a lower incidence of IVH in a small study sample of 19 SGA neonates when compared with 19 matched AGA neonates with gestational ages below 33 weeks. There was an inverse relationship between gestational age and hemorrhage ($p = 0.0001$).

Serial USGs were planned on the

third, seventh and fourteenth day. However, this protocol could not be followed very strictly mainly due to financial constraints. In all, 313 USGs were done on 218 neonates in the NICU. In 63 neonates, who had serial USGs on 3rd and 7th day of life, 94% of the bleeds (15 out of 16) were detected on the first USG on the third day. These findings are consistent with those described by Volpe(6). Partridge(5) finds the fourth to seventh day as the optimal timing for doing an USG. No new bleeds occurred after the seventh day in our study. One neonate with Grade II hemorrhage showed ventriculomegaly on the fourteenth day, but this infant died with gastroenteritis soon after going home. Unfortunately, there were no survivors with Grades III and IV hemorrhage and no comments can be made regarding the development of hydrocephalus.

USG at 40 weeks post conceptual age was done in 99 infants to see if this could be used as a prognostic indicator for neurodevelopmental outcome. Nwaesei(7) did USG examinations at 1,2,3,6 weeks after birth and then at term. He found the USG at 40 weeks to have the best predictive value for outcome. Bilateral periventricular leucomalacia with cysts has a sinister prognosis(8). In our study, the worst outcome was seen in an infant who had periventricular leucomalacia with cystic changes. This infant developed spastic quadriplegia and was severely mentally handicapped. Four children who had a normal USG in the NSCU and at term, had delayed mental development, probably because they had associated septicemia. Two children with Grade I bleed in the NSCU and a normal USG at term also had developmental delay. No other

cause for this delayed development could be found.

Many studies(2,5) have Reported only short term neurological outcome with a one year follow up. Cooke *et al.* have reported a much longer follow up of 2-5 years(8). We have shown in our longitudinal follow up of preterm infants(17) that AGA preterm infants catch up with normal controls at 18 months, while as SGA infants may take as long as 24 months to catch up in their mental development. Hence, the group of 9 infants who had developmental quotients between 70-84 at 1 year were followed up for a further period of 12 months. Three infants caught up, while as 6 continued to show delayed mental development. These children may turn out to be "slow learners" when they start school.

Ours is a referral hospital and neonates are referred to us from a 250 km radius. It was very difficult for us to recall these small babies for a USG at term from such a distance. We could recall only 72 babies who lived in the vicinity of our city for the one year assessment.

The sensitivity and positive predictive value is low in our study compared to others(7,8). This is due to the small number of infants with positive findings on USG at term. However, the specificity of USG at term for prediction of neurodevelopment was 89.2% and the negative predictive value was 90%. This indicates that normal ultrasonographic findings at term correctly predict a good neurodevelopmental outcome.

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