"EVALUATION OF CEREBRAL ARTERY BLOOD FLOW PATTERN IN PREMATURE BABIES AND ITS CORRELATION WITH NEUROLOGICAL ABNORMALITIES – A CROSS SECTIONAL OBSERVATIONAL STUDY"

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IN

PAEDIATRICS

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LIST OF ABBREVIATIONS USED

ACA	–	anterior cerebral artery
CBFV	–	cerebral blood flow volume
CNS	–	central nervous system
CT	–	computer tomography
CVH	–	cerebro ventricular haemorrhage
GMH	–	germinal matrix haemorrhage
IPE	–	intraparenchymal echogenicities
IVF	–	in vitro fertilization
IVH	–	intraventricular haemorrhage
LSCS	–	lower segment caesarian section
MCA	–	middle cerebral artery
MRI	–	magnetic resonance imaging
PCA	–	posterior cerebral artery
PI	–	pilsatality index
PIVH	–	peri intraventricular haemorrhage
PVL	–	periventricular leukomalacia
RI	–	resistance index
USG	–	ultrasonography

ABSTRACT

Background and objectives:

Of all the pregnancies, about 10% end in preterm labour and of these preterm babies about 10% sustain neurological injuries. The present study was undertaken with objective to study the cerebral blood flow using colour Doppler in premature babies and its clinical correlation. Also, to evaluate the possible use of determining cerebral blood flow for predicting prognosis and outcome at the end of the study.

Methods:

A total of 60 preterm babies born prior to 37 weeks of gestation and those with abnormal neurological presentations were included in this study. Neurosonogram was carried out within 72 hours of life.

Results:

The commonest clinical manifestation in preterm babies in our study was seizures (10%) and delayed cry (10%). Neurosonogram study performed within 3 days of birth showed abnormal neurosonogram findings in 6 babies and rest of the 54 babies showed normal neurosonogram study. The most common abnormality found on neurosonogram was germinal-matrix haemorrahge, hydrocephalus, periventricular leukomalacia comprising 3% of cases each. In our study out of the 14 babies who suffered perinatal asphyxia 10 cases had low RI. Of the 2 babies with IVH and 2 babies with hydrocephalus, it was found that all the babies had increased RI.

Conclusion:

Neurosonogram is the best initial method of investigation for preterm babies with suspected neurological injuries. It is best to perform neurosonogram studies on preterm babies within 1st week of birth. . It is non- invasive, non- ionising, widely available, cheap, and repeatable.

Keywords :

Preterm babies; cerebral blood flow; RI index; neurological abnormalities

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INTRODUCTION

Neuroimaging assessment of premature babies is becoming increasingly important as the number of premature births is increasing and survival rate of very low birth weight babies is also increasing and survivors remain at great risk for neurodevelopment impairments.[1]

Approximately 10% of newborns are born prematurely. Of these children more than 10% will sustain neurological injuries leading to significant learning disabilities, motor developmental delay, cerebral palsy, seizures and mental retardation.[2]

Several types of brain injuries may occur secondary to hemodynamic alterations in premature infants including white matter injury, germinal matrix hemorrhage, intra ventricular hemorrhage, periventricular leukomalacia and cerebellar hemorrhage and atrophy.

The hemodynamic instability associated with preterm birth is related to these brain injuries as 40% have their onset within 5 hours of birth and 90% within the first 4 days. They are unusual after 34 weeks of gestation.[3]

Neonatal sonography of the brain is now an essential part of new born care, particularly in high risk and unstable premature infants. Current ultrasound technology allows for rapid evaluation of infants in intensive care nursery with virtually no risk.[4]

CT is not typically used in the premature infant because of the instability of the infant and the lack of good grey / white matter differentiation from the high water content in the newborn brain.

The advantages of sonography over computed tomography (CT) / magnetic resonance imaging (MRI) include portability, lower cost, speed, no ionizing radiation, and no sedation. Screening of premature infants for intracranial hemorrhage has proven highly sensitive and specific. Ultrasound is essential for the neonatal evaluation and follow up of hydrocephalus and periventricular leukomalacia (PVL).[4]

OBJECTIVES

1. To study cerebral blood flow using colourdoppler in premature babies and its clinical correlation.
2. To evaluate the possible use of determining cerebral blood flow, for predicting prognosis and outcome at the end of the study.
3. To correlate various clinical presentations with neurosonographic findings.
4. To study the role of neurosonogram in detecting lesions like germinal matrix hemorrhage, intraventricular hemorrhage, periventricular leukomalacia and others in preterm neonates.

REVIEW OF LITERATURE

Sonography of head was first performed in 1955 and involved the use of A-mode to detect midline structure and obtain a crude estimation of ventricular size.[5]

In 1963, two-dimensional bidirectional echoencephalogram appeared and was a significant technical advance since it provided better information about ventricular size, as well as intracranial spatial relationships.[6]

With the advent of the Octoson and sector-format real-time ultrasonic instruments, two-dimensional imaging of infant head became a reality. Resolution and image display is equal to that obtained with computerized tomography and in some cases appears to be superior.[7]

In 1980, sonography was recommended as the primary technique for detecting intracranial hemorrhage in preterm neonates. This technique is both sensitive and specific for subependymal germinal matrix hemorrhage, intraventricular hemorrhage, and ventriculomegaly. Satisfactory studies can be performed at the bedside with little risk to the infant.[8]

A prospective study of 25 consecutive premature infants less than 1,500 g was undertaken to evaluate the frequency and sonographic appearance of subependymal germinal matrix hemorrhage. In all 12 sonographically positive cases, the hemorrhage was initially imaged in the area immediately anterior to the caudothalamic groove. Special attention to this area permits early detection of germinal matrix hemorrhage, and neurosonography of neonates should be considered incomplete unless this area has been thoroughly imaged.[9]

In a study done over a 14-month period, 112 consecutively born neonates with a birth weight between 1,501 and 2,000 g were screened by cranial ultrasonography. Nineteen patients (17%) had abnormal scans. Of these abnormalities, 14 (13%) were germinal matrix hemorrhage and/or intraventricular hemorrhage. More than half of the hemorrhages identified were severe, ie, grades III and IV.[10]

Neurosonogram was performed on 96 infants weighing 1500 g or less over a 9-month period. Intracranial subependymal / intraventricular hemorrhage occurred in 22 (23%) of the infants. Of these 13 (59%) developed ventricular enlargement, the ventricular enlargement developed within 2 weeks of the hemorrhage in 77% of cases.[11]

In a prospective study of 49 neonates delivered less than or equal to 32 weeks gestation, the initial hemorrhage typically occurred in the first three days of life, with 36% occurring on day 1, 32% on day 2, and 18% on day 3.By the sixth day, 91% of all intracranial hemorrhage had occurred.[12]

In a study of 75 infants weighing less than 2,000 g at birth the findings demonstrate that with extensive IPE there is little or no chance for survival with normal neurologic and cognitive outcome, but with localized IPE, although major motor deficits are common, an appreciable proportion of infants have cognitive function in the normal range.[13]

In a retrospective study of 742 premature neonates evaluated over a 3-year period, study concluded that intracranial hemorrhage occurred in 44% of patients with 20% being Grade 1, 10% Grade 2, 7% Grade 3, and 7% Grade 4. All hemorrhages occurred during the first week of life.[14]

In prospective study of 75 preterm infants of 34 weeks gestation or more and birth weight above 1500 g (range 1500 g to 2500 g), all neonates were screened by cranial ultra-sonography for evidence of peri-intraventricular hemorrhage (PIVH).

Sonographic abnormalities were detected in 16(21.3%) of patients. Intracranial hemorrhage was frequently associated with a low Apgar score, need of resuscitation and/or assisted ventilation immediately after birth.[15]

In a prospective study of 124 neonates of less than 1250 g birth weight by cranial sonography, IPE occurred both early, at 36 hours or before , and later, i.e., between 48 and 96 hours. Study concluded that in GM-IVH and IPE were noted simultaneously in neonate with the earlier onset IPE (diagnosed within 36 hours); GM-IVH preceded the IPE by 6 to 48 hours when the lesion was of a later onset.[16]

In a prospective study done on 499 preterm infants, demographic features of infants screened in the 1st vs. 2nd week of life were similar, more patients screened in the 1st week had questionable PVL diagnosed. Study concluded that routine screening may be delayed until the 2nd week without compromising patient care. Widespread use of a similar screening protocol would result in significantly fewer studies being performed, reducing the cost.[17]

In the only prospective assessment of the ability of these two modalities to predict outcome at 3 years, van de Bor and colleagues found MR imaging did not do better than cranial sonography. This was largely because both modalities detected the most severe lesions, and most children with milder lesions on MR imaging had normal outcome. If the concern when counseling parents is to alert them when a serious adverse outcome is likely in their child, then cranial sonography is to be favored precisely because it is less able to detect subtle lesions, which the developing brain has the capacity to overcome.[18]

In a prospective study of 146 preterm infants (< 2,200 g), the incidence of GMH in those weighing less than 1,501 g, was 36%. GMH occurred mainly in the

first week of life (65%) and in 70% of cases was classified as grade I. Risk factors found to be related to the GMH were hypoxia and excessive handling .[19]

In September 2002, Rezaie P and Dean A, studied that those generally considered to be at greatest risk for PVL are premature, very low birth-weight infants. It is estimated that approximately 3-4% of infants who weigh less than 1,500 g (3.3 lb) have PVL, and 4-10% of those born prior to 33 weeks of gestation (but who survive more than three days postpartum) have the disorder.[20]

From a cohort of 641 consecutive preterm infants with a birth weight of <1500g, 36 infants with IVH grade 3 and/or 4 were identified. A control group of 69 infants, closely matched for gestational age and birth weight, was selected. Maternal factors, labor and delivery characteristics, and neonatal parameters were collected in both groups. Results of cranial ultrasound examinations, whether routine or performed in presence of clinical suspicion, were also collected. High fraction of inspired oxygen in the first 24 hours, pneumothorax, fertility treatment (mostly IVF), and early sepsis were associated with an increased risk of IVH.[21]

In a prospective study of Cranial ultrasound examination performed between 48 and 96 h of age on 580 neonates of 25–42 weeks gestation, the study concluded that the incidence of cerebroventricularhaemorrhage (CVH) in infants less than 32 weeks gestation was 37%, compared with an incidence of 2.7% in infants of 32 weeks or more.[22]

Colour doppler study has been used in several studies to determine cerebral blood flow velocity in intracranial cerebral arteries of asphyxiated newborns[23,24,25].

The sound waves were given off by the transducer are reflected and their frequency travels proportionally to the velocity of circulating red blood cells in the vessels, thus the peak systolic and diastolic pressures are measured[24]. In 1976,

Pourcelot[25] introduced the concept of RI (resistive index), which is calculated by the formula: RI =(S-D)/S where S and D stand for systolic and diastolic pressures respectively. RI measues vascular resistance. A high RI corresponds to vasoconstriction and low blood flow velocity, wheras low RI is related to vasodilation and high blood flow velocity.

Tsuji et al[26], demonstrated that approximately half of those newborns with abnormal cerebral blood flow will have white matter lesions or intraventricularhaemorrhage, wheras those with a normal cerebral blood flow only 13% will develop these complications.

In a study conducted by NayaraAngollo, Ines Lessa, Suely Ribeiro[27] on cranial Doppler RI in preterm newborns with cerebral white matter lesions, those newborns with hypoxic ischemic cerebral injury, the cerebral blood flow have been initially low, with a high RI on Doppler ultrasound. Here RI was associated with greater severity of complications, but not with death. An abnormal RI result within 72 hours of life was associated with 64.2% of complications related to outcome. A high RI corresponds to vasoconstriction and low blood flow velocity, wheras low RI is related to vasodilation and high blood flow velocity. Therefore RI is an important parameter that should be assessed.

ANATOMY:

An understanding of brain development and anatomy is vital for interpretation of neuroradiological studies.

BRAIN DEVELOPMENT:

The central nervous system (CNS) appears at the beginning of the 3rd week as a slipper-shaped plate of thickened ectoderm, the neural plate. This plate is located in the middorsal region in front of the primitive gut. Its lateral edges soon become elevated to form the neural folds. These neural folds become more elevated, approach each other in the midline, and finally fuse, thus forming the neural tube.[23]

By the fourth week of gestation, three vesicular dilations develop at the rostral portion of the neural tube, thereby defining the forebrain (prosencephalon), midbrain (mesencephalon), and hindbrain (rhombencephalon).

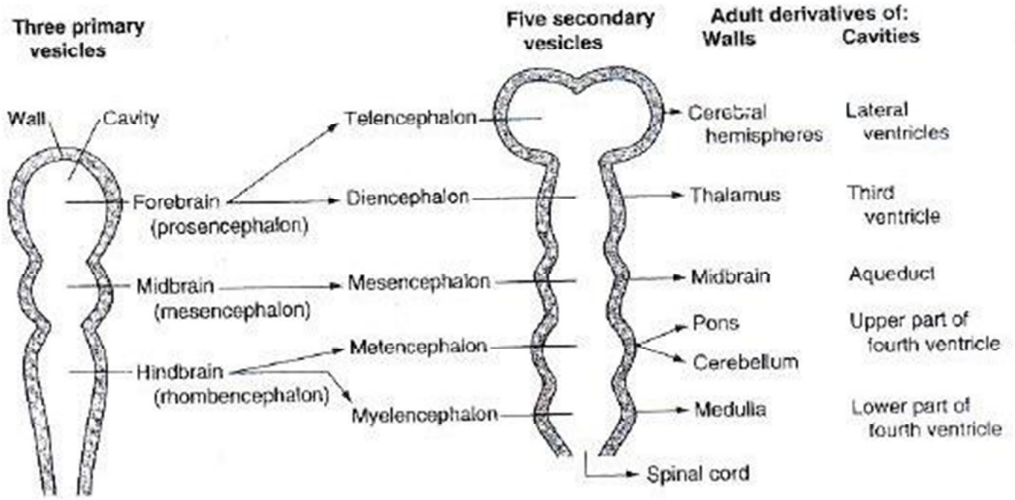


Fig.1 : Diagrammatic sketches of the brain Vesicles indicating the adult derivatives of their walls & cavities

By the fifth week of gestation, the developing forebrain has divided into a cephalic telencephalon and a caudal diencephalon. The developing hindbrain has similarly subdivided into a cephalic metencephalon and a caudal myelencephalon.

The metencephalon later becomes the pons and cerebellum while the myelencephalon forms the medulla oblongata.[24]

Bilateral diverticula from the telencephalic end of the neural tube form the cerebral hemispheres. These hemispheres undergo complex expansion and folding with formation of permanent primitive fissures by the fourth month. Three major flexures, the midbrain, pontine and cervical flexures divide the developing brain into the cerebrum, cerebellum and spinal cord.

Early in development the cerebral hemispheres are smooth-surfaced (lissencephalic), and a germinal matrix of primitive cells surrounds each lateral ventricle. Cells from this germinal matrix proliferate, migrate outward to the cortex in an 'inside out' sequence, and mature as neural and glial cells. The germinal matrix forms at about 7 weeks' gestational age and involutes at about 28 to 30 weeks, although it persists in the form of focal cell clusters up to weeks 36 through 39.[25]

During the sixth and seventh fetal months, the cerebral surfaces convolute to form primitive gyri and sulci. Thus, the adult pattern can already be recognized toward the end of gestation. Concomitant with cortical development is the formation of fiber tracts, including the commissures between the two cerebral hemispheres. The newborn brain constitutes 13% to 15% of the total weight of the body, while the adult brain averages only 2% of the total body weight, weighing about 1400g.

GROSS ANATOMY:

The brain lies in the cranial cavity and is continuous with the spinal cord through the foramen magnum. It is covered by three layers of meninges, namely dura matter, arachnoid and pia matter from outside to inside. The brain is conventionally divided into three major divisions. These are, in ascending order from the spinal cord, the hindbrain, the midbrain, and the forebrain. The hind brain is subdivided into the medulla oblongata, the pons, and the cerebellum. The forebrain is also divided into the diencephalon, which is the central part of the forebrain, and the cerebrum.[26]

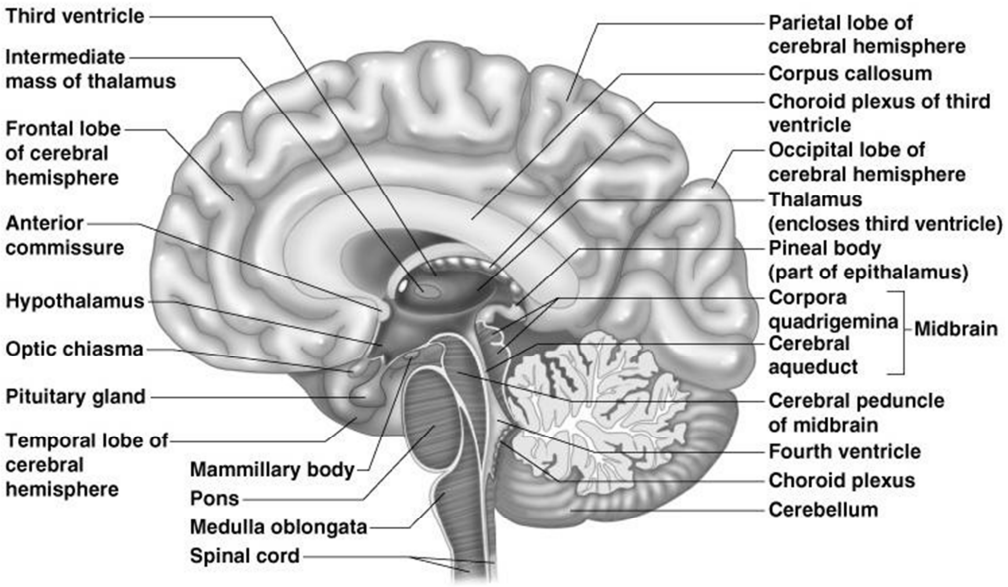


Fig. 2 : Median Sagittal Section of the Brain to show Gross Anatomy.

1. MEDULLA OBLONGATA: is conical in shape and connects pons superiorly to the spinal cord inferiorly. It contains many nuclei and serves as a conduit for ascending and descending nerve fibers.

2. PONS: is situated on the anterior surface of the cerebellum, inferior to the mid brain and superior to the medulla oblongata. It also contains many nuclei and ascending and descending nerve fibers.

3. CEREBELLUM: is situated posterior to the pons and the medulla oblongata in the posterior cranial fossa. It consists of two hemispheres connected by a median portion, the vermis. The cerebellum is connected to the midbrain by superior cerebellar peduncles, to the pons by the middle cerebellar peduncles, and to the medulla by the inferior cerebellar peduncles. The surface layer of each hemisphere is called cortex and is composed of gray matter. The cortex is thrown into folds, or folia, separated by closely set transverse fissures. Certain masses of gray matter are embedded in white matter; the largest of these is known as the dentate nucleus.

MIDBRAIN: is the narrow part of the brain that connects the forebrain to the hindbrain. It contains many nuclei and bundles of ascending and descending nerve fibers.

FOREBRAIN:[26]

1. DIENCEPHALON: is completely hidden from the surface of the brain. It consists of dorsal thalamus and a ventral hypothalamus. The thalamus is a large egg-shaped mass of gray matter that lies on either side of the third ventricle. The hypothalamus forms the lower part of the lateral wall and the floor of the third ventricle.

2. CEREBRUM: is the largest part of the brain and consists of two cerebral hemispheres, which are connected by a mass of white matter called the corpus callosum. The hemispheres are separated by a deep cleft, the longitudinal fissure, into which projects the falxcerebri. The surface layer of each hemisphere, the cortex, is composed of gray matter. The cerebral cortex is thrown into folds, or gyri, separated by fissures, or sulci. A number of the large sulci are conveniently used to subdivide the surface of each hemisphere into lobes. These lobes are named from the bones of the cranium under which they lie.

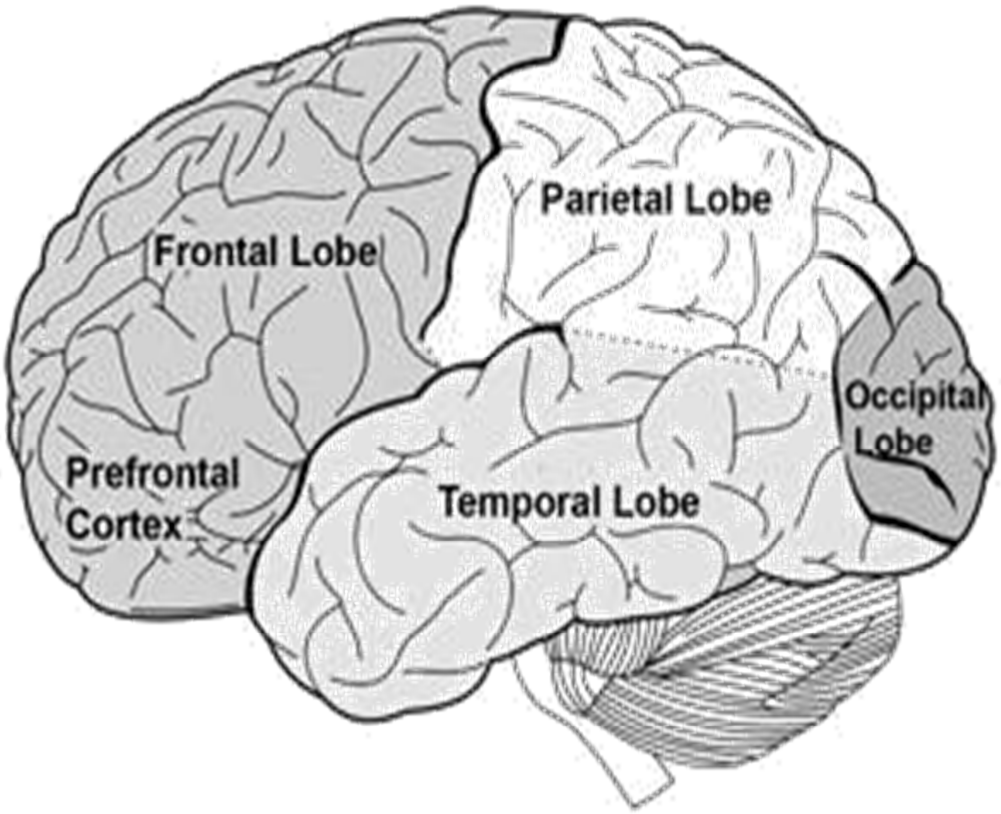


Fig. 3 : Cerebral hemisphere showing the lobes.

Within the hemisphere is a central core of white matter, containing several large masses of gray matter, the basal ganglia. A fan-shaped collection of nerve fibers, termed the corona radiata, passes in the white matter to and from the cerebral cortex to the brainstem. The corona radiata converges on the basal ganglia and passes between them as the internal capsule. The tailed nucleus medial to the internal capsule is referred to as the caudate nucleus and the lens-shaped nucleus on the lateral side of the internal capsule is called the Lentiform nucleus. The lentiform nucleus consists of Putamen in its antero-superior part, and Globus pallidus in its postero- inferior part.

VENTRICULAR SYSTEM:[26]

Ventricles are the cavities within the brain which contain the cerebrospinal fluid (CSF) and choroid plexus. There are two lateral, one third and one fourth ventricles. The two lateral ventricles are present in cerebral hemispheres and

communicate through the formina of Monro with the third ventricle. The third ventricle is a slit like cleft present between the two thalami. It communicates with the fourth ventricle through the cerebral aqueduct of Sylvius. The fourth ventricle is present posterior to the pons and medulla and anterior to the cerebellum. It communicates with the subarachnoid space through the three foramina in its roof andcontinues distally with the central canal of spinal cord.

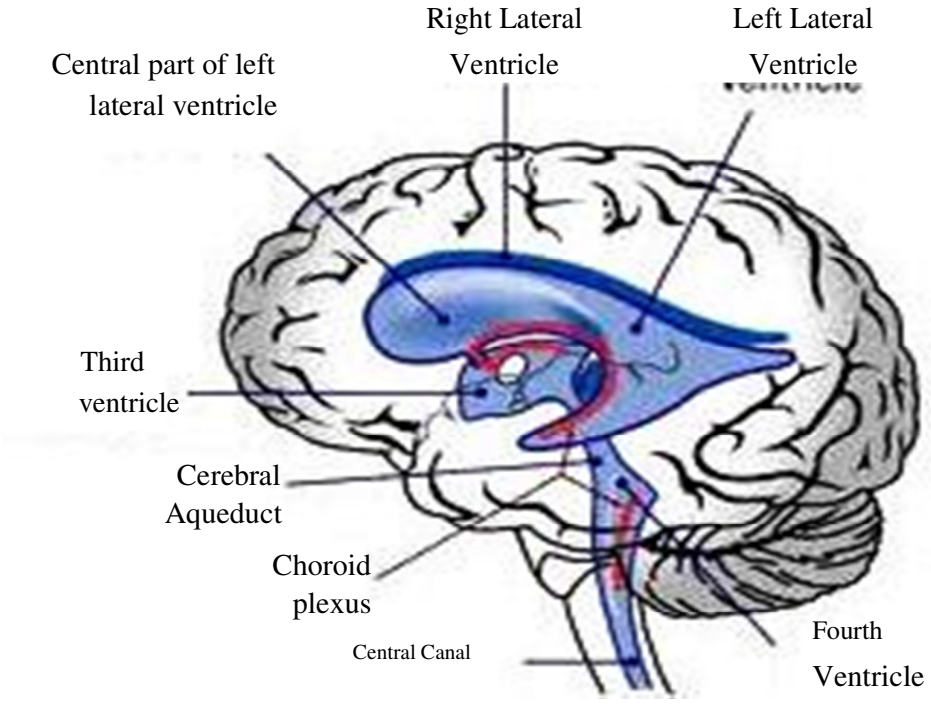


Fig. 4: The ventricular system of the human brain

Choroid plexus is a specialized structure which secretes the CSF. CSF flows through the ventricles and subarachnoid space, and supports the central nervous system. CSF is absorbed primarily through the arachnoid villi into the superior sagittal sinus.

BLOOD SUPPLY OF THE BRAIN:[26]

1. ARTERIES OF THE BRAIN:

The brain is supplied by the two internal carotid and the two vertebral arteries. All these arteries and their branches anastomose on the inferior surface of the brain to form the circle of Willis.

a) Internal Carotid arteries: The intra cranial part of the internal carotid arteries divides into anterior and middle cerebral arteries.

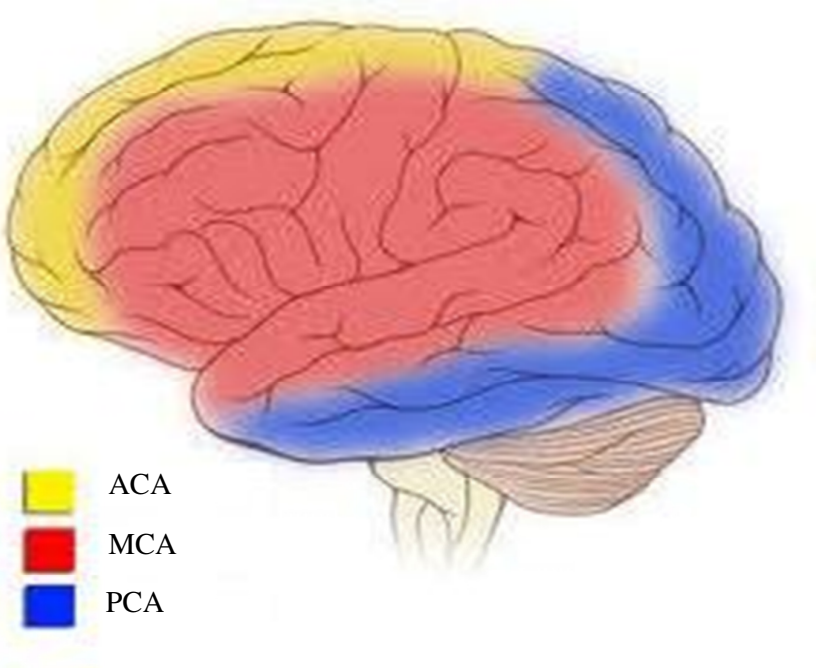


Fig. 5 : Cortical territories of the three cerebral arteries.

The anterior cerebral artery (ACA) supplies the medial surface of the cerebral hemisphere from the frontal pole to the parieto-occipital sulcus. The penetrating branches of the ACA supply the anterior portion of the putamen and caudate nucleus and the antero-inferior part of the internal capsule. The middle cerebral artery (MCA) supplies the lateral convexity of the cerebral hemisphere. The penetrating branches of MCA supply the internal capsule, caudate nucleus, putamen and globuspallidus.

b) The vertibrobasilar arteries: The two vertebral arteries join to form the basilar artery. The basilar artery divides into two posterior cerebral arteries (PCA). The PCA supply the midbrain, thalamus, lateral and medial geniculate bodies, occipital lobe and inferior surface of the temporal lobe. The other branches of the vertibrobasilar arteries supply pons, medulla, cerebellum and anterior part of spinal cord.

2. VEINS OF THE BRAIN:[26]

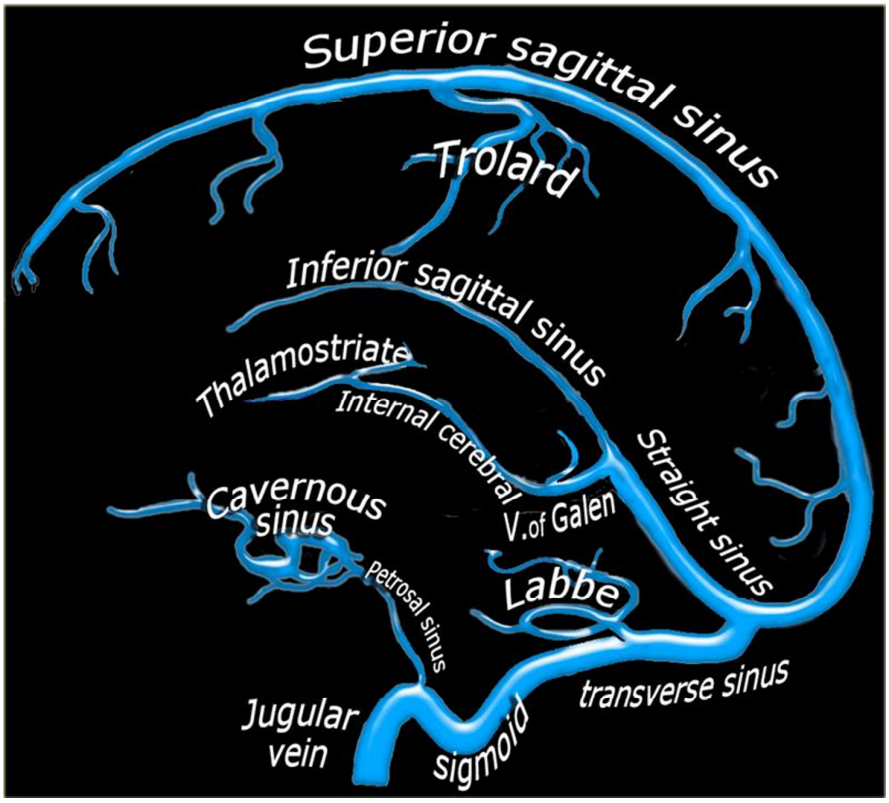


Fig. 6 : Cerebral hemisphere to show the venous anatomy.

The cerebral veins are divided into two groups: superficial (cortical) and deep veins. The superficial or cortical veins mainly drain the lateral surface of the cerebral hemispheres into the cavernous and superior sagittal sinuses. The deep cerebral veins include medullary veins, subependymal veins, the basal veins and the vein of Galen. They mainly drain the deeper layers of cerebral hemisphere into the straight sinus.

NORMAL ULTRASONIC APPEARANCE OF NEONATAL BRAIN:

Thorough knowledge of normal ultrasonic anatomy of neonatal brain is essential in order to utilize ultrasound to diagnose and evaluate the various conditions that affect the brain.

In premature infants, the surface of the brain is smooth because the gyri and sulci are underdeveloped. The subarachanoid spaces are prominent in very premature infant, causing the sylvian fissure to be almost square, whereas later, after infolding of the insula (operculization) it becomes a narrow echogenic fissure filled with middle cerebral artery branches.[27]

Lateral ventricles:

Asymmetry of the lateral ventricles is a common variant. More often, the left ventricle is larger than the right, the occipital horns are larger than the frontal horns.

The ventricles of the premature infant are usually larger than those of term infant, they appear as fluid filled comma-shaped structures.[28]

Caviseptipellucidi and vergae :

The cavumseptipellucidi is seen in the midline between the anterior horns of lateral ventricles. The posterior part of the cavum septum pellucidi is termed cavumvergae.

The cavumvergae is interposed between the bodies of the lateral ventricles. The foramen of Monro marks the dividing line between these two parts of the cavum.

Choroid plexus:

The choroids plexus is responsible for producing CSF in the ventricles. It lines the body as well as the occipital and temporal horns of each lateral ventricle. The largest part of the choroids plexus, which is known as glomus, is in the trigones of the lateral ventricles.

At the level of the glomus, the choroids plexus tapers as it courses anteriorly to the roof of the third ventricle and posteriorly into the temporal horns of each lateral ventricle. Choroid plexus ends at the caudothalamic groove and it never extends into the frontal or occipital horns of the lateral ventricles.[28]

Germinal matrix:

The germinal matrix develops deep to the ependyma and consists of loosely organized, proliferating cells that give rise to the neurons and glia of the cerebral cortex and basal ganglia. Its vascular bed is the most richly perfused region of the developing brain. Vessels in this region form an immature vascular rete of fine capillaries, extremely thin- wall veins and larger irregular vessels.

Although germinal matrix is not visualized on sonography, it is important as the typical anatomic site that lies above the caudo-thalamic groove and beneath the ependymal lining of ventricles where hemorrhage occurs in preterm infants.[4]

Periventricular white matter echogenicity:

An echogenic band paralleling the posterior part of the lateral ventricles is a normal finding seen in virtually all neonates. This band of echogenicity is referred to as periventricular halo. The degree of echogenicity should be less than or equal to that of normal choroid plexus. The halo should have a homogenous brush like appearance. The differential of periventricular echogenicity includes cerebral hemorrhage and

periventricular leukomalacia. Either of these conditions should be suspected if the periventricular halo is symmetric or more echogenic than choroid plexus.[28]

CROSS-SECTIONAL SONOGRAPHIC ANATOMY:[27,28,4]

The echofree ventricular system, echogenic sulci, nuclei and septa and the pulsatile intracranial major arterial branches serve as landmarks for identifying the normal structures within the brain in coronal, sagittal and parasagittal views.

Coronal view :

The anatomy in the coronal plane will be described in six sections, as seen when the ultrasonic transducer is swept from the frontal to the occipital regions.

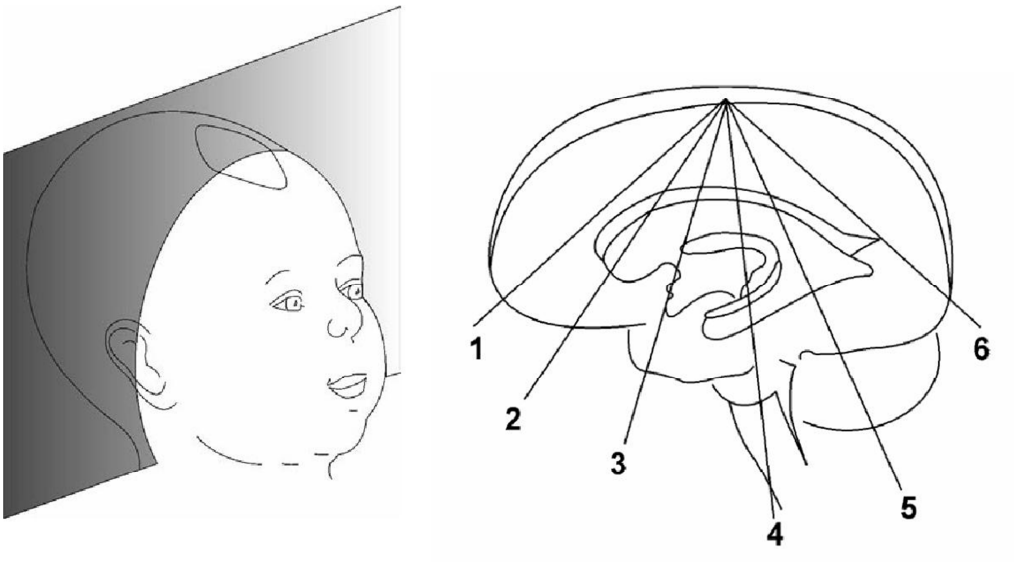


Fig. 7 : Standard Coronal planes

Coronal plane 1 :

The most anterior image is acquired just anterior to the frontal horns of the lateral ventricles. Visualisation of the anterior cranial fossa is obtained, including the frontal lobes of the cerebral cortex with the orbits deep to the floor of the skull base.

Coronal plane 2 :

Moving posteriorly, the frontal horns of the lateral ventricles appear as symmetrical, anechoic, comma shaped structures with the hypoechoic caudate heads within the concave lateral border. Structures visualized from superior to inferior in the midline include interhemispheric fissure, cingulate sulcus, genu and anterior body of corpus callosum and septum pellucidum between the ventricles. Moving laterally from the midline, the caudate nucleus is separated from the putamen by internal capsule. Lateral to the putamen, the sylvian fissure is echogenic because it contains middle cerebral artery.

Coronal plane 3 :

Progressing farther posteriorly to the level above the midbrain, the body of the lateral ventricles is seen on either side of the cavumseptipellucidi. Below this, the thalami lie on either side of the third ventricle.

Coronal plane 4 :

A slightly more posterior transducer angulation results in a plane that includes the cerebellum. The body of the lateral ventricles becomes more rounded. At this level in the midline, the body of the corpus collosum is deep to the cingulate sulcus, and the third ventricle is located between the anterior portions of the thalami.

Echogenic material visualized in the floor of the lateral ventricles is the choroids plexus. Echogenic choroids plexus is also seen in the roof of the third ventricle, resulting in three echogenic foci of choroids.

Below this, in the posterior fossa, vermis is the echogenic structure in the midline surrounded by more hypoechoic cerebellar hemispheres.

Coronal plane 5 :

Further posteriorly, the trigone or atrium of the lateral ventricles and occipital horns are visualized. The extensive echogenic glomus of the choroids plexus nearly obscures the lumen of CSF filled ventricle at the trigone. Inferiorly the cerebellum is separated from the occipital cortex by the tentorium cerebelli.

Coronal Plane 6:

The most posterior section visualizes predominantly occipital lobe cortex and the most posterior aspect of the occipital horns of the lateral ventricles that do not contain choroids plexus. This section is angled posterior to the cerebellum.

Sagittal imaging:

The sagittal images are obtained by placing the transducer longitudinally across the anterior fontanelle and angling it to each side.

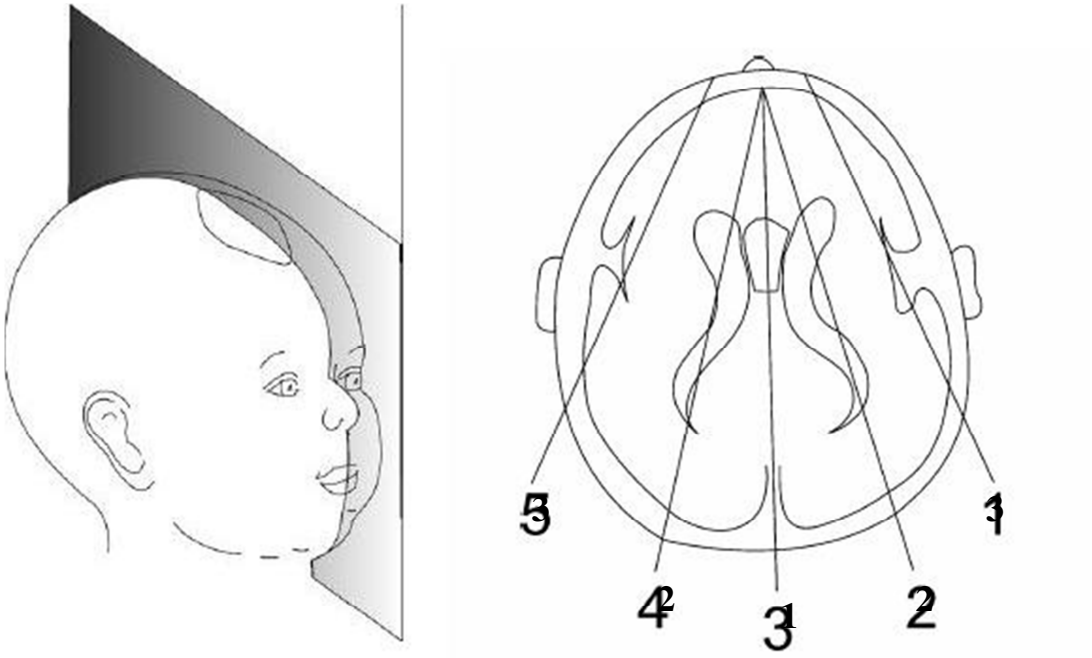


Fig. 8 : Standard sagittal planes

Midline sagittal plane :

The midline is first identified through the interhemispheric fissure by recognition of the curving line of the corpus collosum above the cystic cavumseptipellucidi and cavumvergae, the third and fourth ventricles and the highly echogenic cerebellar vermis. The cingulate sulcus lies parallel to and above the corpus collosum.

Above the lateral ventricle is the cerebral cortex, and below it is the cerebellar hemisphere. The caudate nucleus and the thalamus are within the arms of the ventricle. The caudothalamic groove at the junction of these two structures is an important area as it is the most common site for germinal matrix hemorrhage in the subependymal region of the ventricle.

Parasagittal planes (through lateral ventricles and insulae.): More pronounced lateral angultion will demonstrate the peripheral aspect of the ventricles and the more lateral cerebral hemisphere, including the temporal lobes. Where middle cerebral artery branch extend toward the ventricle parasagittal view almost always demonstrates a normal hyperechoicperitrigonal blush just posterior and superior to ventricular trigones.

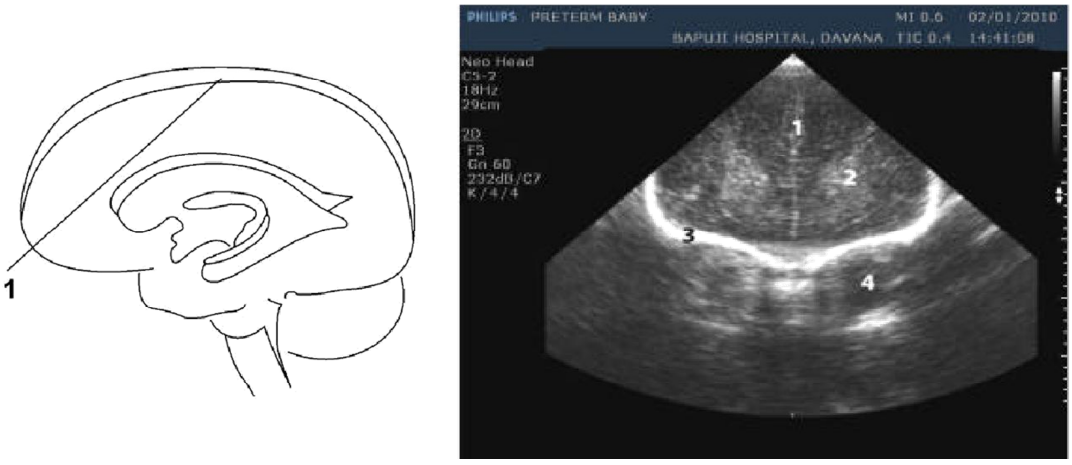


Fig. 9 : First coronal plane (C1) at the level of the frontal lobes

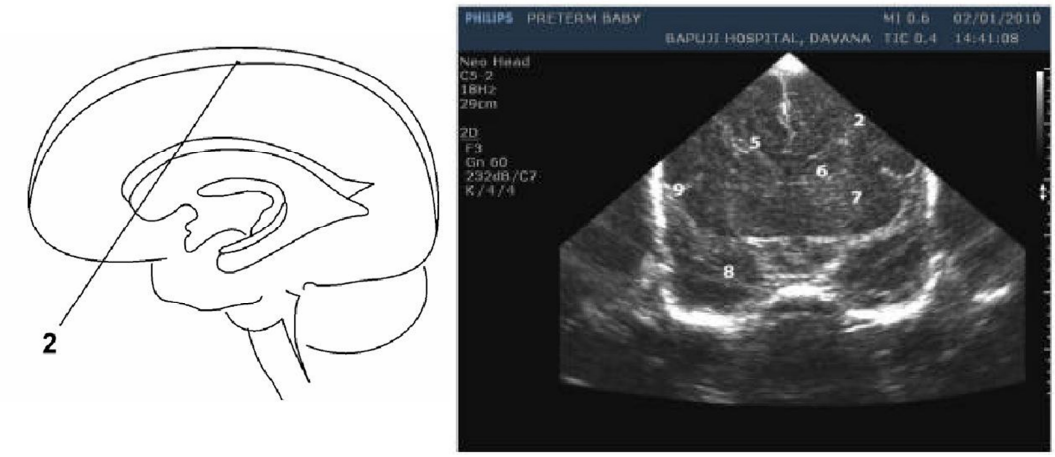


Fig. 10 : Second coronal plane (C2) at the level of the frontal horns of the lateral ventricles.

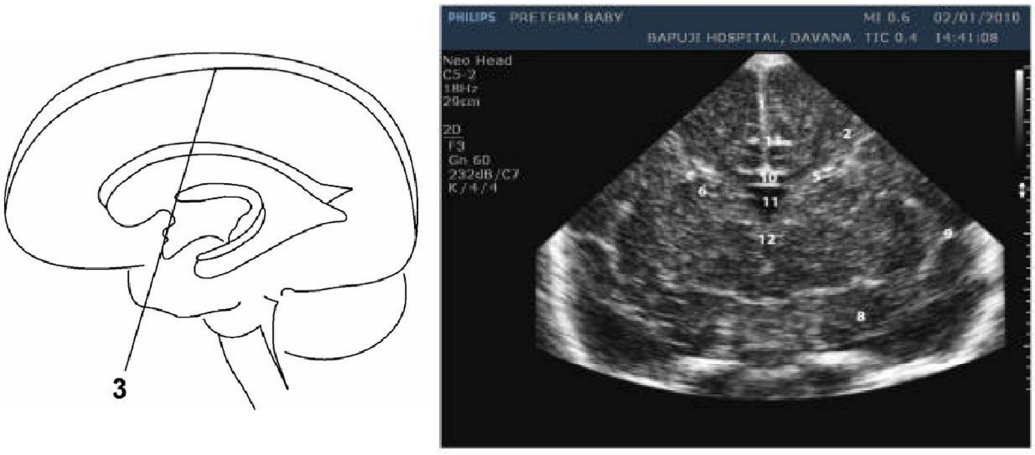


Fig. 11 : Third coronal plane (C3) at the level of the foramen of monro and the third ventricle.

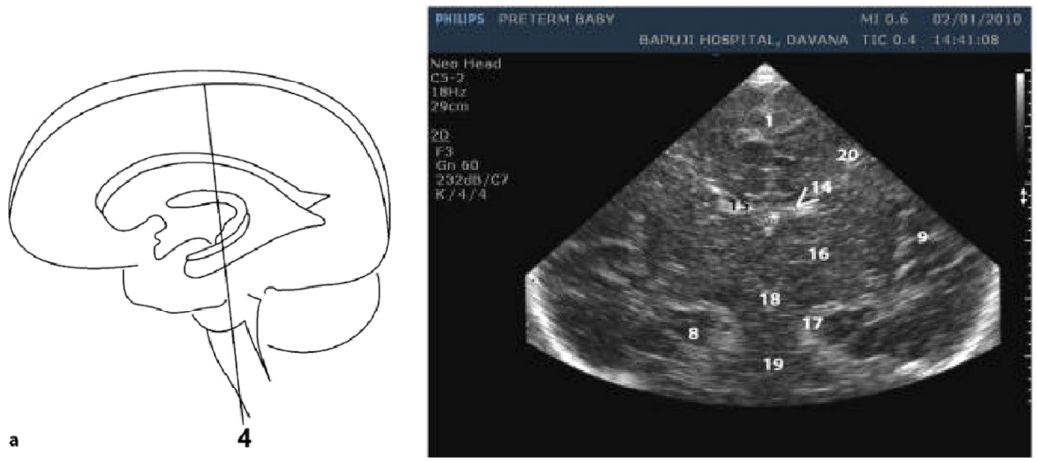


Fig. 12 : Fourth coronal plane (C4) at the level of the bodies of the lateral ventricles.

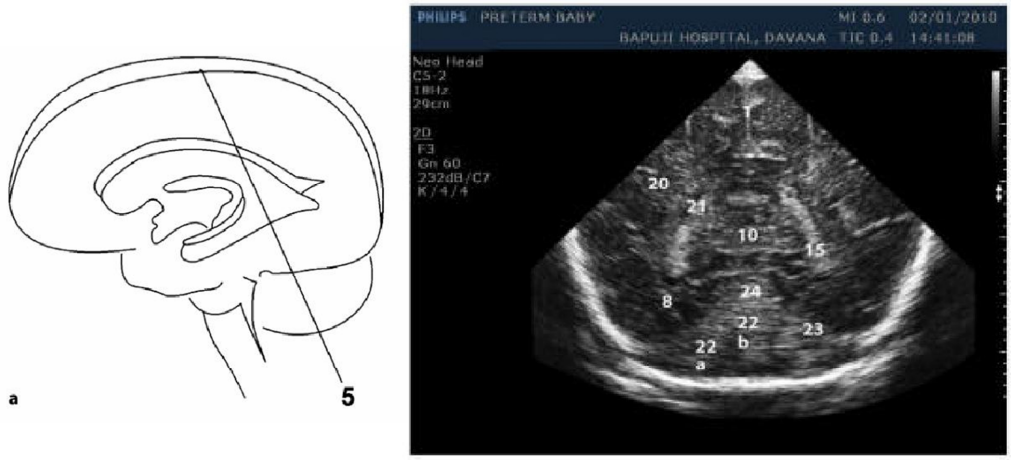


Fig. 13 : Fifth coronal plane (C5) at the level of the trigone of the lateral ventricles.

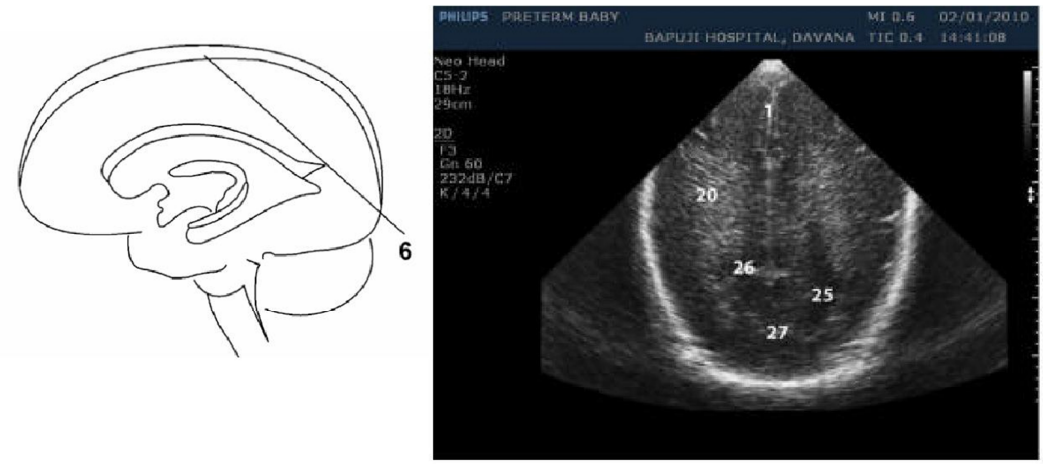


Fig. 14 : Sixth coronal plane (C6) through the parieto-occipital lobes.

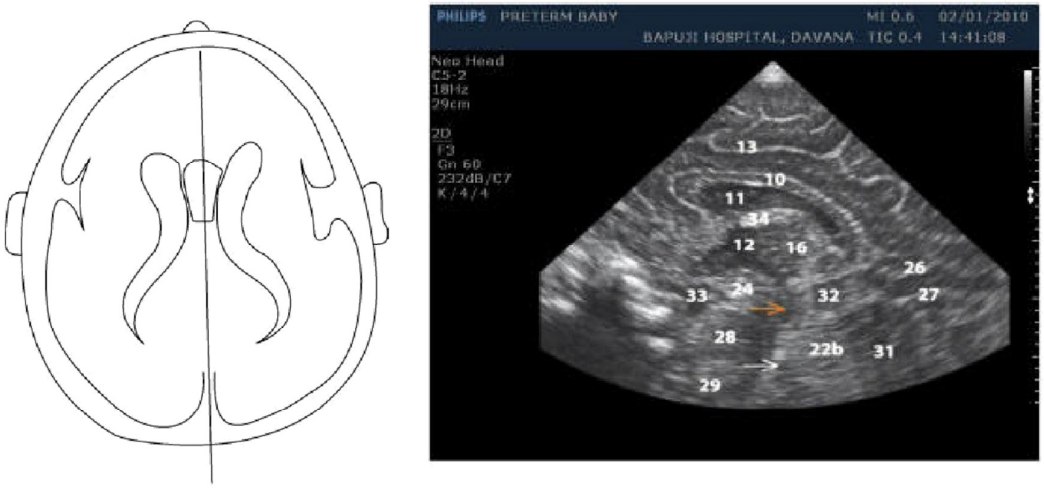


Fig. 15 :Midsagittal plane through the third and fourth ventricles.

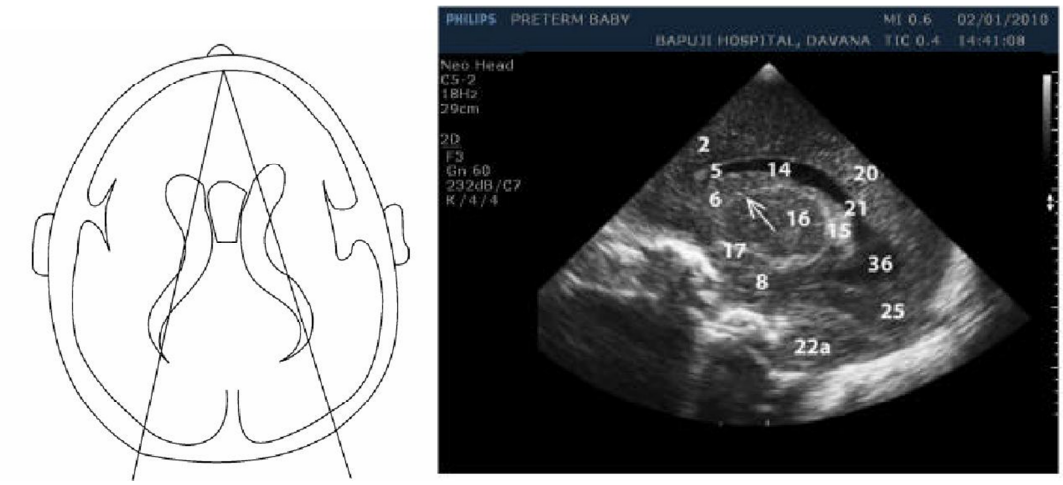


Fig. 16 : Parasagittal planes throug h the right and left lateral ventricles.

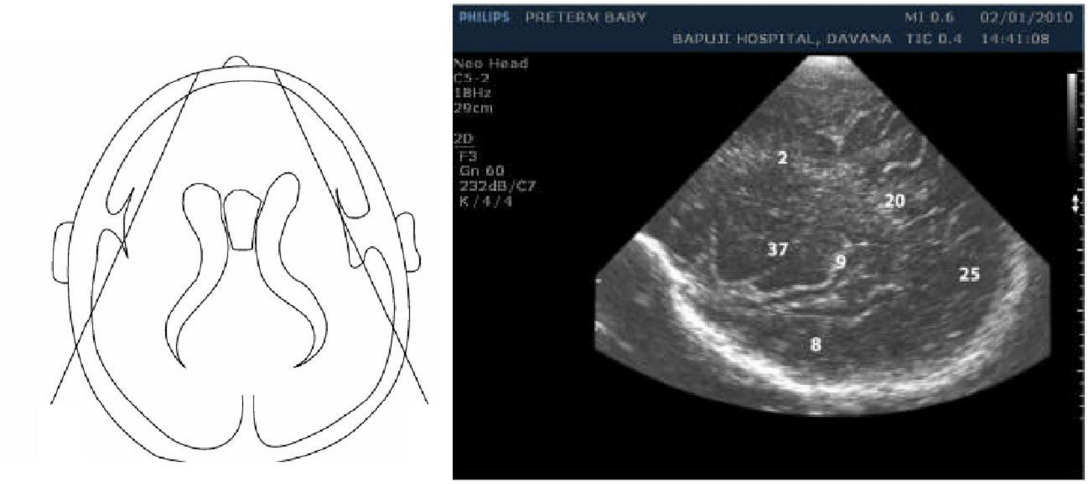


Fig. 17 : Parasagittal planes through the insulae (right and left).

Legends of Corresponding Numbers in Ultrasound Scans

1. Interhemispheric fissure	23.	Tentorium
2. Frontal lobe	24.	Mesencephalon
3. Skull	25.	Occipital lobe
4. Orbit	26.	Parieto-occipital fissure
5. Frontal horn of lateral ventricle	27.	Calcarine fissure
6. Caudate nucleus	28.	Pons
7. Basal ganglia	29.	Medulla oblongata
8. Temporal lobe	30.	Fourth ventricle
9. Sylvian fissure	31.	Cisterna magna
10. Corpus callosum	32.	Cisterna quadrigemina
11. Cavum septum pellucidum	33.	Interpeduncular fossa
12. Third ventricle	34.	Fornix
13. Cingulate sulcus	35.	Internal capsule
14. Body of lateral ventricle	36.	Occipital horn of lateral ventricle
15. Choroid plexus	37.	Insula
22. Cerebellum		

Regulation of cerebral blood flow (CBF)

The brain is supplied by four large arteries: two internal carotid (ICA) and two vertebral arteries. Each internal carotid artery arises from the common carotid artery in the neck and divides into the anterior cerebral (ACA) and the middlecerebral (MCA) arteries. The first branches of the left and right subclavian arteries are the vertebral arteries, which ascend through the neck to the brainstem and formthe basilar artery (BA) at the level of the pons. The BA branches into two posterior cerebral arteries. The internal carotid arteries and BA divide into several branches and form an anastomotic structure called the Circle of Willis.

The ACA and the MCA provide blood to the frontal and parietal lobes, themajor area of the temporal lobe and deep grey matter. Blood to the cerebellum and brain stem is supplied by the branches of the BA, except for parts of thecerebellum and medulla oblongata which are supplied by the branches of the vertebralarteries. The BA supplies blood to a part of the temporal lobe, the occipital lobe andthe thalamus. The posterior cerebral artery supplies the inferior surface of the brain and the occipital lobe.

At term neonatal CBF varies between 10 and 20 mL/100g/min and representsapproximately 40% of adults values. CBF increases with postnatal age in parallel with the increasing cerebral metabolic rate and energy demand of the growing brain[34] (Chalak et al. 2014a). The cerebral circulation is regulated by a number of homeostatic mechanisms, including autoregulation, the arterial partial pressure of CO_2($PaCO_2$) and O_2 (PaO_2), blood glucose, neuronal activity[35] (Volpe 2008), blood viscosity and flow-metabolism coupling on the CBF[36] (Udomphorn et al. 2008).

Autoregulation

Cerebral autoregulation is a homeostatic mechanism where arteries dilate and constrict to maintain CBF near constant over a broad range of perfusion pressures,known as the autoregulation plateau[37,38,39] (Greisen 2005, Liem and Greisen 2010,Tasker 2013).

Autoregulation maintains a constant CBF if the mean arterial pressure (MAP)is within certain limits (approximately 24 to 39 mmHg) in preterm infants of gestational age between 24 to 30 weeks[40] (Tyszczuk et al. 1998). Although the meanarterial pressure limits of the autoregulation plateau have not been established, theapproximate autoregulatoryrange ranges lies between 25 mmHg and 50 mmHg. The upper and lower limits of MAP vary according to gestational age[35] (Volpe 2008).

It has been recommended that the MAP in mmHg should not fall below the gestational age of the infant in weeks to maintain autoregulation (Joint Working Party of the British Association of Perinatal Medicine and the Research Unit of the Royal College of Physicians 1992). Beyond these limits of the autoregulation plateau, CBF depends on MAP in a pressure-passive manner, which means that hypotension results in cerebral ischemia and hypertension causes cerebral hyperemia[36] (Udomphorn et al 2008). A pressure-passive cerebral circulation is frequent in premature infants in the first days after birth. It is not, however, an "all-or-none" phenomenon. In very-low-birth-weight (VLBW) preterm infants, CBF monitored by NIRS (near-infrared spectroscopy) is reported to be pressure-passive for an average of 20% of the recording time. Impaired cerebral autoregulation is associated with low gestationalage and birth weight, systemic hypotension and maternal hemodynamic factors in preterm infants of birth weight less than 1500 g[41] (Soul et al. 2007).

The deficit is considered to be a risk factor for ischemic brain injury in preterm infants[42] (Khwaja and Volpe 2008), but the role of impaired autoregulation in the development of IVH has not been established[43] (Ballabh 2014). The autoregulation of CBF has been found using Xenon clearance or Doppler ultrasonography to be impaired in full-term infants with asphyxia. Cerebral hyperemia after asphyxia is common, and is associated with a poor outcome[44,45,46] (Archer et al. 1986, Pryds et al.1990a, Boylan et al. 2000).

Other regulatory factors

Carbon dioxide (CO_2) is the most potent cerebral vasodilator. CBF is sensitive to changes in $PaCO_2$[36,38,39,47] (Udomphorn et al. 2008, Liem and Greisen 2010, Tasker2013, Vutskits 2014). The hypercapnia induced increase in CBF is approximately 6% per mmHg change in $PaCO_2$, and hypocapnia reduces CBF by

approximately 3% per mm Hg change in $PaCO_2$[39] (Tasker 2013). Hypercapnia> 55 mmHg (> 8 kPa) is associated with impaired cerebral autoregulation in VBLW infants (Kaiser et al2005). The association between PVL and severe hypocapnia is well documented[48,49,50](Greisen et al. 1987, Okumura et al. 2001, Shankaran et al. 2006). Even mild hypocapnia (< 4.5 kPa) is associated with leukomalacia and CP in preterm[51](Collins etal. 2001) and with poor outcome after HIE in term infants[52](Pappas et al. 2011).

The influence of PaO2 on the cerebral circulation is of lesser clinical significance. There are minimal changes in CBF with changes in PaO2 above 50mmHg (6.7 kPa). Below a PaO2 threshold of 50 mmHg (7 kPa), CBF increases to maintain adequate cerebral oxygen delivery[36,39] (Udomphorn et al. 2008, Tasker2013).The arterial oxygen concentration is related not only to PaO2 but also to the hemoglobin concentration and the oxygen affinity to hemoglobin. Oxygen delivery to the brain may be affected not only by hemoglobin concentration, but also by the blood viscosity[35] (Volpe 2008).

In a recent Doppler study term infants with polycythemia had significantly lower blood flow velocity in MCA, whereas infants with anemia had significantly higher cerebral blood flow velocity (CBFV) compared to normocythemic infants[53] (Weissman et al. 2012). Preterm infants with anemia have increased CBF, while in polycythemia CBF decreases as measured by NIRS[54] (Liem et al. 1997).

Hypoglycemia (< 1.7 mmol/L) has been shown to increase CBF in preterm infants to maintain glucose supply to the brain[55] (Pryds et al. 1990b). Immature vascular anatomy is also one of the important determinants of CBF in newborns[56] (Brew et al. 2014).

Neuronal activation

Further research is needed on the impact of neuronal activation, seizures or drug-induced central nervous system depression on infants' cerebral hemodynamics or metabolism[56] (Brew et al. 2014). However, coupling of neuronal activity to CBF has been reported in sleep states and seizures. A decrease in CBF during sleep in preterm[57] (Greisen et al. 1985) and a marked increase in CBF with the neuronal activity of aseizure in asphyxiated term infants[58] (Perlman et al. 1985) have been reported.

BRAIN INJURIES IN PRETERM BABIES:

Preterm infant is an infant born at less than 37 completed weeks or 259 days of gestation. Preterm birth is a major determinant of neonatal mortality and morbidity and has long term adverse consequences for health.

Children who are born prematurely have higher rates of cerebral palsy, sensory deficits, learning disabilities and respiratory illnesses compared with children born at term. The morbidity associated with preterm birth often extends to later life.

The neurologic manifestations of brain injury in the premature infant range from the less severe morbidity and cognitive deficits to major spastic motor deficits, including spastic diplegia and spastic quadriplegia with more profound intellectual deficits.

Of all the neonatal deaths (i.e., deaths within first 7 days of life) that are not related to congenital malformations, 28% are due to preterm birth.[30]

Incidence and etiology :

- World-wide the preterm birth rate is estimated at 9.6% representing about 12.9 million babies.
- Incidence of preterm birth in India is approximately 21%.

Although the incidence of germinal matrix hemorrhage was as high as 55% previously, the incidence of PVL was 25-40% in babies born less than 32 weeks gestational age and in very low birth weight infants.

Recent reports of GMH range from 10-25% and incidence of PVL has decreased to 7% due to increased usage of antenatal steroids and improved neonatal respiratory care such as surfactant therapy.[31]

Multiple factors have been studied as cause for GMH. Common associations include prematurity with complications such as hypoxia, hypertension, hypercapnia, hypernatremia, rapid volume increase and pneumothorax. PVL is anticipated to follow maternal chorioamnionitis and severe hemodynamic insult like cardiorespiratory compromise resulting in hypotension and severe hypoxia and ischaemia.[31]

PATHOPHYSIOLOGY:[3]

Brain damage in preterm infants may result from a series of events rather than one specific insult. Maturational characteristics with a failing adaptation capacity may predispose the brain to harmful events during both intrauterine and extrauterine life.

Structural and functional immaturity of the organs responsible for ventilation and circulation in a preterm infant is the basic reason leading to lack of an acceptable cerebral blood flow and arterial oxygen delivery in the brain under unfavourable clinical conditions.

Immature vascular structures, certain developmental characteristics in the cerebral circulation, intrinsic cell vulnerability and various toxic mechanisms overlap and contribute to predisposition to cerebral damage.

ARTERIALWATERSHED DETERMINES REGIONAL PATTERN OF BRAIN DAMAGE IN PRETERM INFANTS :[32]

The immature new born brain has very characteristic angioarchitecture at this age. Normally there is a watershed zone between the ventriculopetal and ventriculofugal arteries. Below 34 weeks of gestation this water shed zone is located in the periventricular area. With increasing maturity the sulci deepen and the course of subcortical and long straight medullary arteries changes from a gentle bend to more acute bend. The watershed area thus moves from preventricular zone to subcortical location. Since the watershed area in preterm is in immediate periventricular region, the germinal matrix hemorrhage and periventricular leucomalacia are common pathological findings.

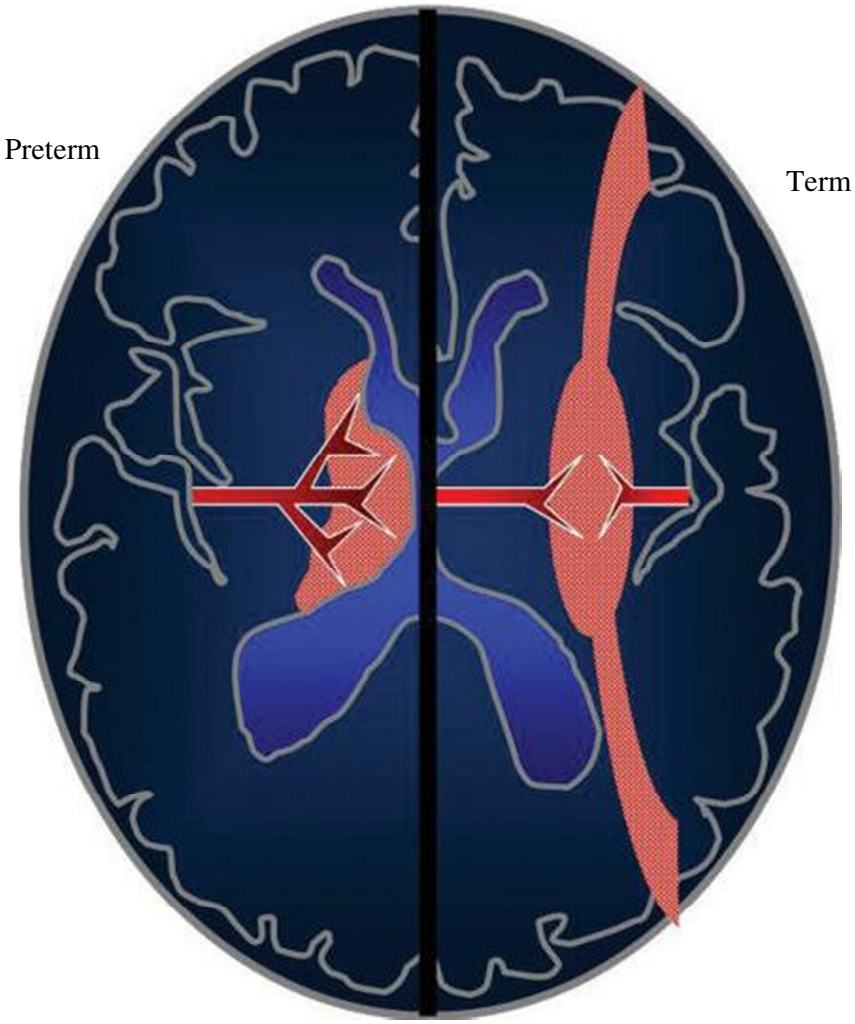


Fig. 18 : The premature neonatal brain (left) has a ventriculopetal vascular pattern. In the term infant (right), a ventriculofugal vascular pattern develops as the brain matures, and the border zone during hypoperfusion is more peripheral[43]

GERMINAL MATRIX HEMORRHAGE :

The germinal matrix is a fine network of blood vessels and primitive neural tissue that lines the ventricular system in the sub ependymal layer during fetal life. As the fetus matures germinal matrix regresses towards the foramen of munro, so that by full term only small amount of germinal matrix is present in the caudothalamic groove.

Sonography is the most effective method for detecting this hemorrhage in the newborn period and for follow up in the subsequent weeks. Most hemorrhage (90%) occurs in the first 7 days of life, but only one third of these occur in the first 24 hours.[34]

The brain of the premature infant lacks the ability to auto-regulate cerebral blood pressure, thus fluctuations in cerebral blood pressure and flow can rupture this fine network of blood vessels which is highly susceptible to pressure and metabolic changes.[4]

The germinal matrix is rarely a site of hemorrhage after 32 weeks of gestation because it has almost disappeared.

Germinal matrix hemorrhage may occur in subependymal, intraventricular or intraparenchymal regions. However, GMH originates predominantly as hemorrhage in the germinal matrix below the subependymal layer and may be contained by the ependyma or may rupture into the ventricular system or less often into the adjacent parenchyma.[33]

The optimal cost-effective timing to screen premature infants is at 1 to 2 weeks of age to identify patients with significant hemorrhage as well as those developing hydrocephalus.[35]

Small subependymal hemorrhages might be missed when screening is done late because they resolve quickly, but these have not proven clinically important.[34]

The classification of GMH most widely used was proposed by Burstein et al.[33]

GRADES OF GERMINAL MATRIX HEMORRHAGE

Grade	Type / Description
I	Subependymal hemorrhage
II	Intraventricular extension without hydrocephalus
III	Intraventricular hemorrhage with hydrocephalus
IV	Intra parenchymal hemorrhage with or without hydrocephalus.

Grade I:– SUBEPENDYMAL HEMORRHAGE :[4]

Neurosonogram show sub ependymal hemorrhage as a region of increased echogenicity. Images acquired in the coronal plane show a well defined area of increased echogenicity adjacent to the ventricular wall. The most common location is at the caudothalamic notch, inferior to floor of frontal horn. Sagittal plane is often very useful in differentiating germinal matrix hemorrhage from the echogenic choroids plexus because choroid plexus does not extend anterior to foramen of munro, whereas caudate head and adjacent ganglionic eminence hemorrhage lie immediately anterior to the foramen.

This subependymal hemorrhage is typically noted in first weeks of life. As the hematoma ages, the clot becomes less echogenic with its centre becoming sonolucent. The clot retracts and necrosis occurs with complete resolution of hemorrhage or occasionally development of a subependymal cyst. It may persist as linear echo adjacent to the ependyma.

GRADE II : INTRAVENTRICUALR HEMORRHAGE.[28]

Grade II hemorrhage results when subependymal blood ruptures through the ventricular wall entering the lumen. It appears as echogenic material within part or all of a non-dilated ventricular system. Most often, the blood accumulates in the dependent part of ventricle (the occipital horns). In some neonates, it can be difficult

to identify small amounts of hemorrhage in a non dilated ventricle, particularly if choroid plexus is large.

Doppler imaging is useful to distinguish normal vascularised choroids plexus from non vascularised clot. Use of posterior fontanellae views helps the detection of small IVH in third and fourth ventricle or CSF blood fluid levels in the occipital horns.[4]

Over the first few weeks after the acute event, the intra ventricular clot organizes and become well defined and less echogenic. At this stage, it appears as a relatively sonolucent mass within the lateral ventricle usually in the body or the atrium. At this time the clot is less echogenic than the choroids plexus which is situated adjacent to the thalamus. As the grade II hemorrhage resolves the ventricular wall often becomes echogenic.[29]

Early onset IVH, in the first 6 hours of life is uncommon and has been associated with higher risk of both cognitive and motor impairment including cerebral palsy.

GRADE III – INTRAVENTRICULAR HEMORRHAGE WITH HYDROCEPHALUS.[4]

Grade III hemorrhage fills and also enlarges one or both lateral ventricles. Because of hydrocephalus, the clot and choroids plexus are better defined. The echogenic clot may be adherent to the ventricular walls or may become dependent within the ventricular wall.

In the acute phase after the intra ventricular hemorrhage, ventricular dilatation results from blockage of the CSF pathways by hemorrhagic particulate matter. This acute hydrocephalus often resolves and is of no prognostic value.

When hemorrhage is severe it can cause obliterativearachnoiditis that usually occurs in the basilar cisterns, the arachonoidal adhesions block the normal flow of CSF and necessitate permanent ventriculoperitoneal CSF diversion.[29]

As the intraventricular clot retracts, echogenic debris or floating clot fragments may be seen in the ventricles.

Patients with post hemorrhagic ventricular dilation have an increased incidence of periventricular white matter injury, pontosubicular injury and olivocerebellar injury.[28]

GRADE IV : INTRA PARENCHYMAL HEMORRHAGE :

Intra parenchymal hemorrhage is usually in the cerebral cortex and located in frontal or parietal lobes, because it often extends from the subependymal layer over the caudo-thalamic groove.

Studies suggest that intra parenchymal hemorrhage is caused by hemorrhagic venous infarction secondary to obstruction of the terminal veins by large subependymal hemorrhage or intraventricular hemorrhage.

Periventricular hemorrhagic infarctions are ischaemic parenchymal injuries associated with hemorrhage that typically occur in deep white matter adjacent to lateral ventricle.[4]

On sonography they appear as globular, cresentic, or fan shaped areas of mixed hyper and hypoechogenicity. As the clot retracts the edges form an echogenic rim around the centre, which becomes sonolucent. The clot may move to a dependent position and by 2-3 months after the injury an area of porencephaly or encephalomalacia develops.[29]

PERIVENTRICULAR LEUCOMALACIA:

Periventricular leucomalacia, the principle ischaemic lesion of the premature infant, is infarction and necrosis of the periventricular white matter.

The pathogenesis of PVL has been found to relate to 3 main factors.

i) Immature vasculature in the periventricular watershed area.

ii) The absence of vascular autoregulation in premature infants.

iii) Maturation dependent vulnerability of the oligodendroglial precursor cell damage in PVC. These cells are extremely vulnerable to attack by free radicals generated in the ischemia – reperfusion sequence.

Pathologically, the periventricular white matter undergoes coagulation necrosis, followed by phagocytosis of the necrotic tissue.[3]

In PVL, the white matter most affected is in the arterial border zones at the level of the optic radiations adjacent to the trigones of the lateral ventricle and the frontal cerebral white matter near the foramen of munro.[33]

The initial sonographic examination in PVL may be normal within 2 weeks of the initial insult, the periventricular white matter increases in echogenecity until it is greater than the adjacent choroids plexus. This increased echogenicity is usually caused by edema from infarction and may also result from hemorrhage (heterogenous flares). 2-4 weeks after the insult, cystic changes may develop in the area of abnormal echogenic parenchyma. The cyst can be single or multiple and are parallel to the ventricular border in the deep white matter. These cysts measure from 5mm to 1-2 cm in diameter. Cystic changes are usually bilateral and symmetrical.[36]

Tissue loss secondary to cavitatory white matter injury results in ventricular enlargement that usually appears towards the end of 2nd week. A late screening for periventricular leucomalacia should be performed to search for cystic changes of PVL and ventricular enlargement which may be missed if the late screening is not done.

Classification of periventricular leucomalacia according to **de vries**.[32]

Grade	Definition
I	Transient periventricular echodensities persisting for 7 days or longer
II	Periventricular echodensities evolving into small localized fronto-parietal cystic lesions.
III	Periventricular densities evolving into extensive periventricular cystic lesions.
IV	Densities extending into deep white matter, evolving into extensive periventricular and subcortical cystic lesions.

Late neurologic problems from PVL include developmental delay and symmetrical spastic diplegia involving both legs, often noticeable by 6 months of age. Spastic diplegia occurs because of the pyramidal tracts from the motor cortex that innervate the legs pass through the internal capsule and travel close to the lateral ventricular wall. Severe cases of PVL will also affect the arms, resulting in spastic quadriplegia and cause vision and intellectual deficits.

CEREBELLAR HEMORRHAGE:[4]

Cerebellar hemorrhage can occur in premature infants because there is germinal matrix in the fourth ventricle. Mastoid fontanelle imaging is now routinely used to visualize the cerebellum in the optimum focal zone to allow cerebellar hemorrhage to be seen and the posterior fossa fully evaluated.

On sonogram, cerebellar hemorrhage produces either ill defined, asymmetric cerebellar echogenicity or focal mass. It can resolve completely or produce an area of encephalomalacia.

Resolution of cerebellar hemorrhage into a cyst in the posterior fossa may allow easier diagnosis. The normal echogenic cerebellum may obscure hemorrhage when acute.

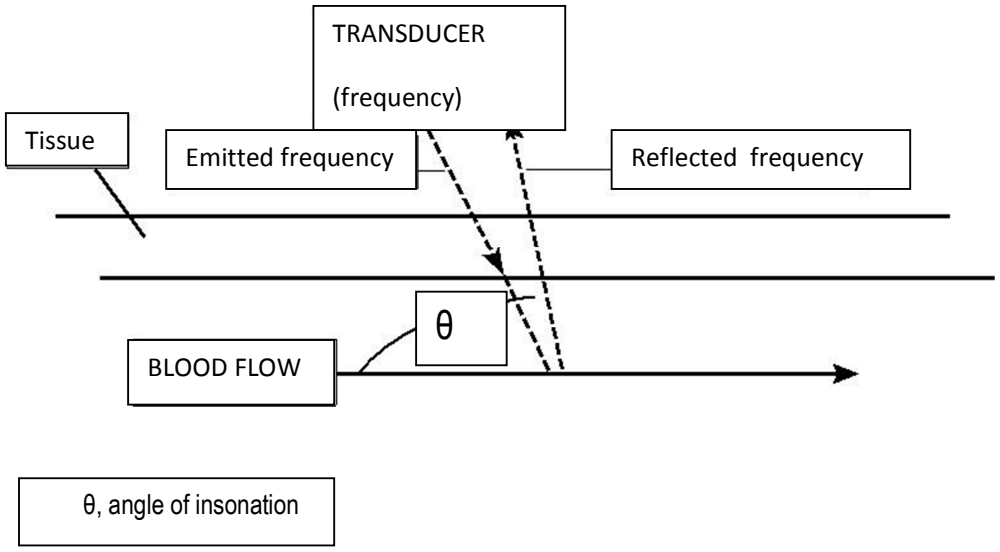
On follow up they develop cognitive deficits and developmental delay without signs of motor abnormalities.

Doppler ultrasonography in the evaluation of CBF

Technical principles

According to the Doppler principle, ultrasound waves emitted from the Doppler transducer are transmitted and reflected by moving red blood cells within the cerebralvessels. The measured Doppler frequency shift is the difference between emitted and reflected waves. (Figure 1.)

Figure 19. The difference in the frequency between the emitted and reflected waves, referred to as the "Doppler frequency shift", is directly proportional to the speed of the moving red blood cells (blood flow velocity).



When the angle of insonation is known and the Doppler frequency shift is measured, the blood flow velocity can be calculated using the formula:

$V = Fd \times c/2 \times Fo \times \cos \theta$, where

V = velocity of blood flow (cm/s)

Fo = emitted frequency (transducer frequency)

Fd = Doppler frequency shift (the difference between emitted and reflected frequency)

c = constant: velocity of sound in brain (1540 m/s)

θ = angle of insonation (angle between emitted ultrasound beam and direction of flow)[67]

(Govaert and de Vries, 2001).

The angle of insonation has an impact on the velocity measured. An angle of zero or the emitted wave parallel to the direction of blood flow (cosine 0 = 1) gives an optimal measurement. The larger the angle, the larger will be the cosine of the angle; the greater the error in blood flow velocity measurement. It is important to minimize the angle of insonation to less than 30 degrees to keep the error below 15%[68] (Purkayastha and Sorond 2012).

The anterior fontanelle is the standard acoustic window in neonatal Doppler and cranial studies. Thereby the ACA, BA and ICA arteries can be identified. The CBFV in the MCA can be measured through the temporal acoustic window[67] (Govaert and de Vries 2001).

Three Doppler indices can be calculated from the cerebral blood flow curve (Figure 2). These indices are angle-independent:S/D ratio = Peak systolic velocity / End-diastolic velocity[69] (Stuart et al. 1980)

Pulsatility index PI = (Peak systolic velocity – End-diastolic velocity) / Mean velocity[70] (Gosling and King 1971)

Resistive index RI = (Peak systolic velocity – End-diastolic velocity) / Peak systolic velocity[71] (Pourcelot 1975).

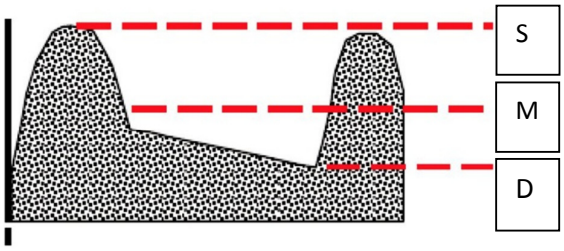


Figure 20.Cerebral blood flow curve by Doppler. Peak systolic velocity (S), mean velocity (M) and end-diastolic velocity (D).

CBF velocity can be used to obtain beat-to-beat changes in systolic, diastolic and mean CBF velocity. The peak systolic CBFV, end-diastolic CBFV and RI are the most common measurements used in monitoring cerebral circulation in infants. An increase or decrease in the CBFVs by Doppler corresponds to an increase or decrease in brain perfusion measured by Xenon-133 clearance[72] (Greisen et al. 1984). A high RI correlates with increased cerebral vascular resistance and a decreased diastolic blood velocity and a low RI with decreased resistance and increased blood velocity in the cerebral diastolic circulation[73] (Lowe and Bailey 2011). Various factors can influence Doppler measurements. Factors which have been shown to affect the cerebral circulation flow velocity in Doppler ultrasonography examinations are presented in Table 1.

	Cerebral blood flow Velocity (CBFV)	Resistive Index (RI)
Intracranial abnormalities		
Intracranial bleeding		Increased
PVL		Increased
Cerebral edema		Increased
Hydrocephalus	Decreased	Increased
Brain death	Decreased	Increased (then no flow)
Asphyxia	Increased	Decreased
Extracranial abnormalities		
PCO2 (hypercapnia)	Increased	Decreased
Heart rate (increased)		Decreased
PDA	Decreased	Increased
Pneumothorax		Increased
Polycythemia	Decreased	Increased
Anemia	Increased	Decreased
Apnea	Decreased	
Seizures	Increased	Decreased
Medications		
Caffeine	Decreased	
Dexamethasone	Increased	
Indomethacin	Decreased	Increased
Surfactant	Increased	

Table 1. Factors and changes in cerebral blood flow velocity and resistive index by Doppler in infants.

Cerebral Doppler ultrasonography in infants

The first neonatal Doppler ultrasonography study was reported in 1979[74] (Bada et al.1979). Normal neonatal reference values and postnatal changes in peak systolic and end-diastolic CBFV have been determined in several studies[75,76,77,78,79,80,81,82] (Gray et al. 1983,Archer et al. 1985, Deeg and Ruprecht 1989, Cheung et al. 1994, Meek et al. 1998, d'Orey et al. 1999, Pezzati et al. 2002, Romagnoli et al. 2006). CBFV increases linearly during the first hours and days of life in both preterm and term infants[78,79,80] (Cheung et al. 1994, Meek et al. 1998, d' Orey et al. 1999) and the velocities increase with gestational age and birth weight[80] (d'Orey et al. 1999). Peak systolic velocities are10-20% higher in the ICA than in the BA or ACA. In contrast to the CBFV, the RI is independent of age and weight[77] (Deeg et al. 1989). There should be no significant differences in RIs among the different cerebral arteries[83] (Bulas 2009). RI ranging between 0.6–0.8 is regarded as normal[77,84] (Deeg et al. 1989, Allison et al. 2000).

Preterm infants

Two different patterns of CBFV by Doppler ultrasonography in premature infants on the first day of life have been observed: (1) a stable CBFV and (2) a fluctuating CBFV (continuous alteration in systolic and diastolic CBFV) pattern. Preterm infants with fluctuating CBFV have had a higher incidence of IVH than infants with stable CBFV patterns[85] (Perlman et al. 1983).

Very low velocities by Doppler also constitute a risk for severe IVH in pretermInfants[86] (Deeg et al. 1990). Low CBFV[87] (Fukuda et al. 2006) and fluctuating CBFV[35](Volpe 2008) in the cerebral circulation are likewise risk factors for developing PVL due to a pressure-passive cerebral circulation. In preterm infants with a symptomatic patent ductus arteriosus (PDA), the diastolic cerebral blood flow has

been seen to decrease because of a ductal stealing effect and cerebral blood flow normalized after closure of PDA[88] (Perlman et al. 1981). Absence of diastolic cerebral blood flow (end-diastolic block) or retrograde diastolic flow in cerebral arteries are associated with hemodynamically significant PDA in preterm infants[89] (Kupterschmid et al.1988) and hydrocephalus with increased intracranial pressure[83] (Bulas 2009).

Loss of diastolic flow, retrograde diastolic flow or no detectable flow in cerebral arteries in a small group of pediatric patients of ages ranging from newborn to 4 years has been related to a high risk of death, although survival without sequela is also possible[90] (Chiu et al. 2003).

METHODOLOGY

A cross-sectional observational study of 60 preterm babies delivered at Shri B. M. Patil Medical College, Hospital and Research Centre, Vijayapur and delivered at outside hospital and referred to our hospital.

Source of data :

Sample for the study are all preterm babies delivered at Shri B M Patil Medical College, Hospital and Research Centre, Vijayapur and delivered at outside hospital and refereed to our hospital

Period of study: January 2014 to August 2015

Selection of patients :

Inclusion criteria :

The study includes :

- Preterm with abnormal neurological presentation seizures, lethargy, apnoea, sudden onset pallor, increase in muscle tone, bulging anterior fontanel.
- All preterm born prior to 37 weeks of gestation.
- All preterm who weigh less than 2500g at birth.

Exclusion criteria :

The study will exclude

All cases suspected to have congenital malformations, severe infections and failed resuscitation.

Preparation of the patient :

- Neonates were examined by wrapping them in warm clothing to maintain normal body temperature.

- Baby was fed adequately before examination.
- No sedation was used
- Baby was laid in supine.
- Hand washing and cleansing of the transducer was done.

Equipment :

All the preterm babies in this study underwent neurosonogram using real time computed ultrasound scanners (SIEMENS Accuson X 700 with high frequency probe VF 12-4 and PHILIPS HD 11 XE with high frequency probe L 12-3).

Sonography technique :

Neurosonographic examinations were performed through anterior fontanelle in both the coronal and sagittal plane.

The examination started in coronal plane along the coronal suture, with transducer angled towards the frontal region. Then brain was examined in various coronal planes by sweeping the transducer from anterior to posterior.

Following the completion of examination in coronal plane, sagittal and parasagittal scans were obtained by placing the transducers on the anterior fontanel, perpendicular to coronal plane and then sweep from midline through the lateral ventricles, lateral parenchyma on each sides.

Care was taken to maintain symmetry throughout the examination, as densely echogenic choroids plexus appear larger on one side causing a false image of subependymal hemorrhage.

Posterior fossa screening was done by obtaining axial images through posterior and mastoid fontanel. Initial neurosonogram was done within 72 hours of birth.

Data analysis:

Determination of sample size:

The sample size n for the desired estimators of the study may be calculated by the following formula with the following assumptions

- Standard deviation of resistance index $\sigma = 0.051$
- $Z\alpha_{/2} = 1.96$ at 5% level of significance
- The permissible error e = 0.01825

$$n = \frac{[Z_{\alpha/2}\ \sigma]^2}{E^2}$$; Z = standard normal variable

E = permissible error (1.8% permissible error for the study based on sample observation)

$$n = \frac{(1.96)^2 \text{ x } (0.051)^2}{(0.01825)^2}$$

$= 30$

Here $[Z_{\alpha/2}]^2 = (1.96)^2 = 3.8416$, the theoretical value of z statistic at 5% level of significance

σ = assumed as standard value from a previous study (article in jornal de perdiatria vol.82,no.3,2006)

Formula for assessment of sample size taken from

BIOSTATISTICAL ANALYSIS – Jerrold H

Statistical tools used:

1. Data presentation is done using bar charts and pie-charts after effective comparison.
2. To assess the presence of association between levels of ACA RI and complications, Chi-square test is used

$$c^2 = \sum_{i=1}^{k} \left[\frac{(O_i - E_i)^2}{E_i} \right]$$

Following chi-square test with (k-1) degrees of freedom

Where, O_i= i^{th} observed frequency

E_i = i^{th} expected frequency

3. The Z- statistic is used to test the significance of the difference between RI levels with steroid and without steroid.

Two-sample z-test	$z = \frac{(\overline{x}_1 - \overline{x}_2) - d_0}{\sqrt{\frac{\sigma_1^2}{n1} + \frac{\sigma_2^2}{n2}}}$

Where, x_1 = mean RI with steroid

x_2= mean RI without steroid

σ_1^2 = variance of RI with steroid

σ_2^2 = variance of RI without steroid

n_1 , n_2 = number of observations with and without steroid respectively

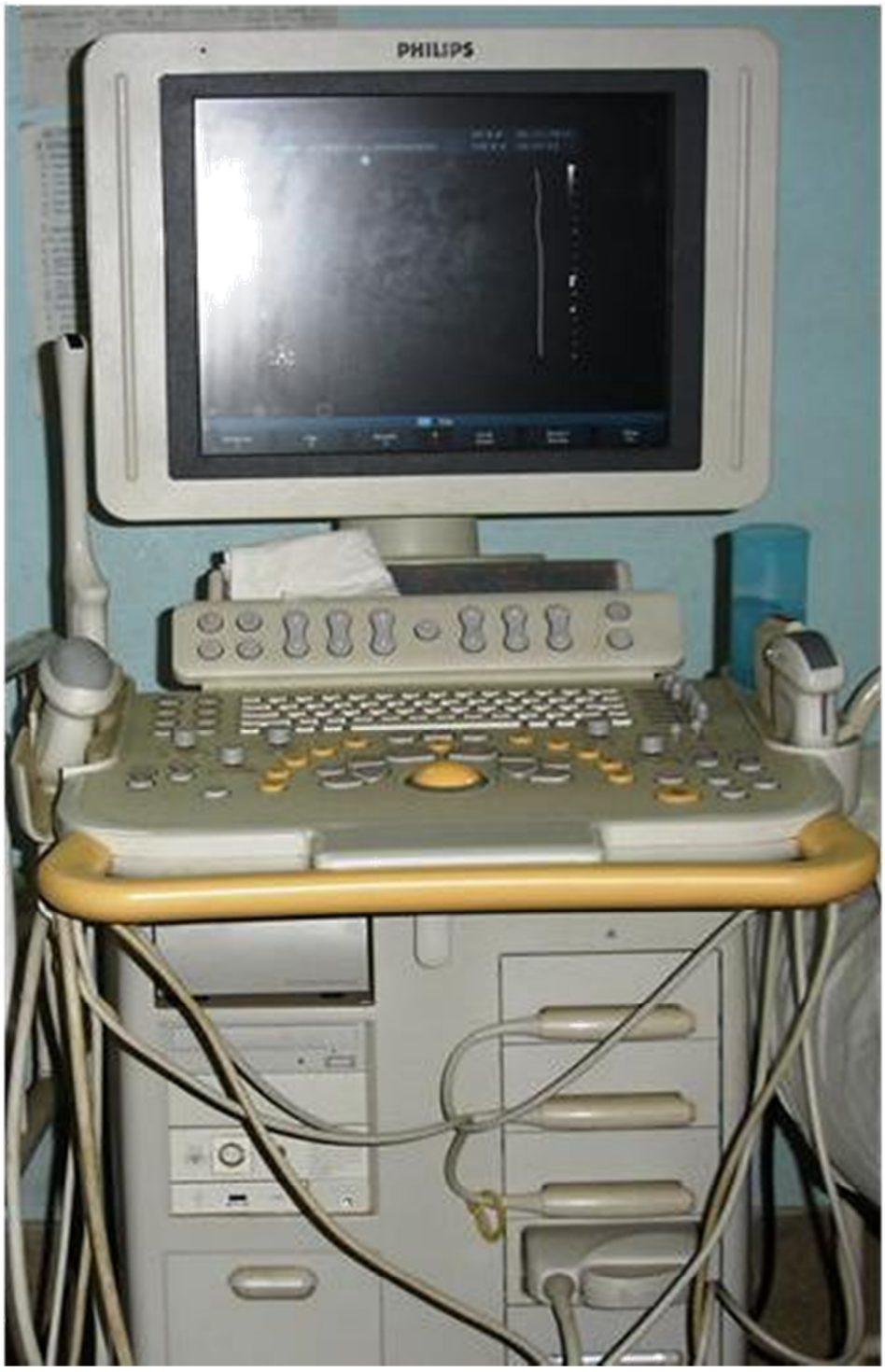


Fig. : Ultrasound equipment : PHILIPS HD 11XE

RESULTS

Our study comprising of 60 preterm showed following results.

Table 1 : Gestational age wise distribution of cases :

Gestational age (wks)	No. of cases	Percentage
28 – 30 wks	4	6.6
30 – 32 wks	20	33.3
32 – 34 wks	24	40
34 – 36 wks	12	20

Table 1 shows maximum cases in the age group of 32-34 wks.

Graph 1 : Gestational age wise distribution of cases

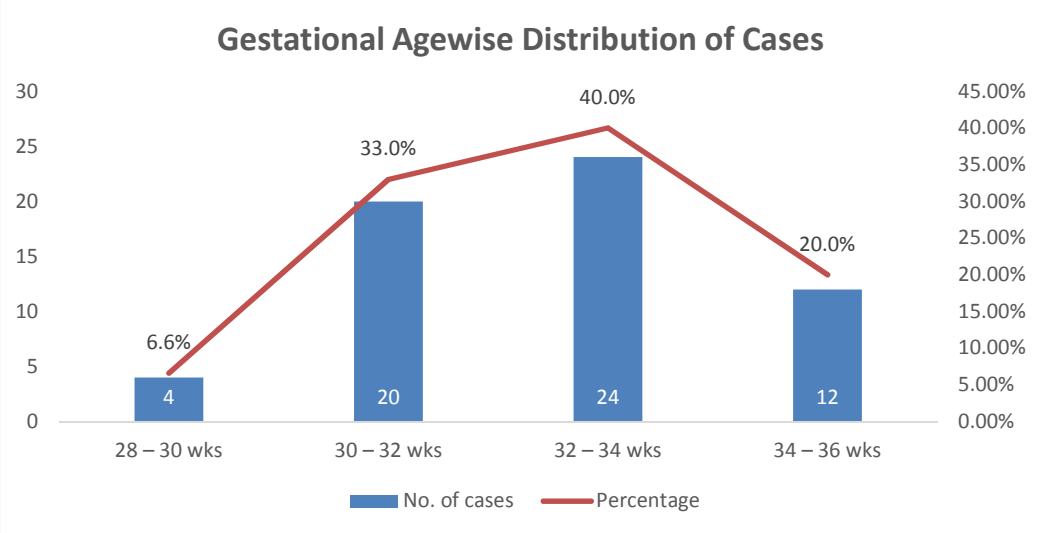


Table 2 : Birth weight

Birth weight (kgs)	No. of cases	Percentage
< 1.5 kg	27	45
1.5 – 2 kg	25	41.6
2 – 2.5 kg	8	13.3
Total	60	100

Table 2 shows majority of cases were in the group of <1.5 kg.

Graph 2 : Birth weight

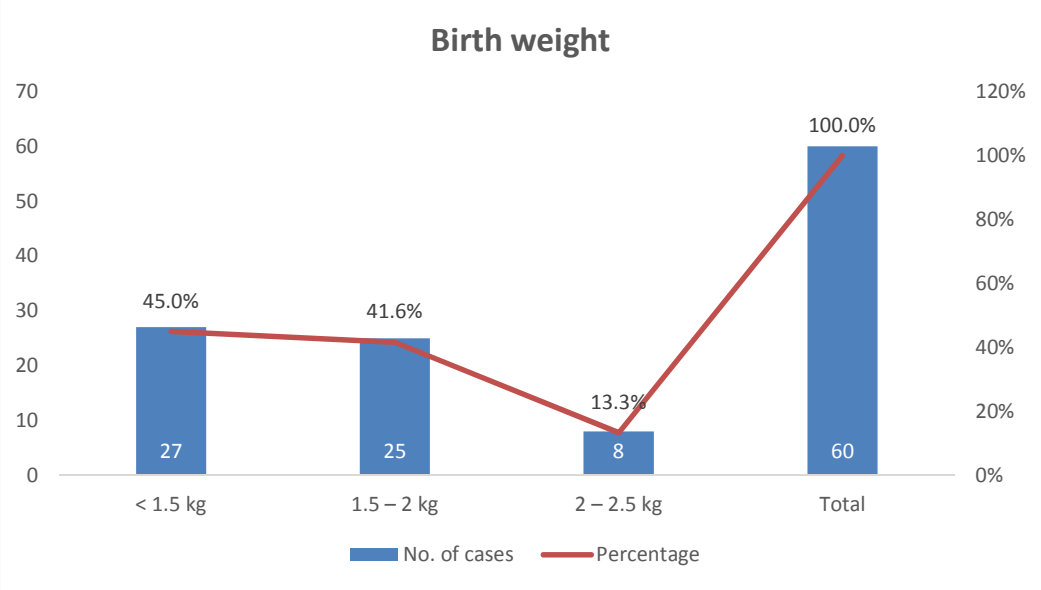


Table 3 : Sex wise distribution of cases

Sex	No. of cases	Percentage
Male	37	61.6
Female	23	38.3
Total	60	100

Table 3 shows maximum cases were males.

Graph 3 : Sex wise distribution of cases

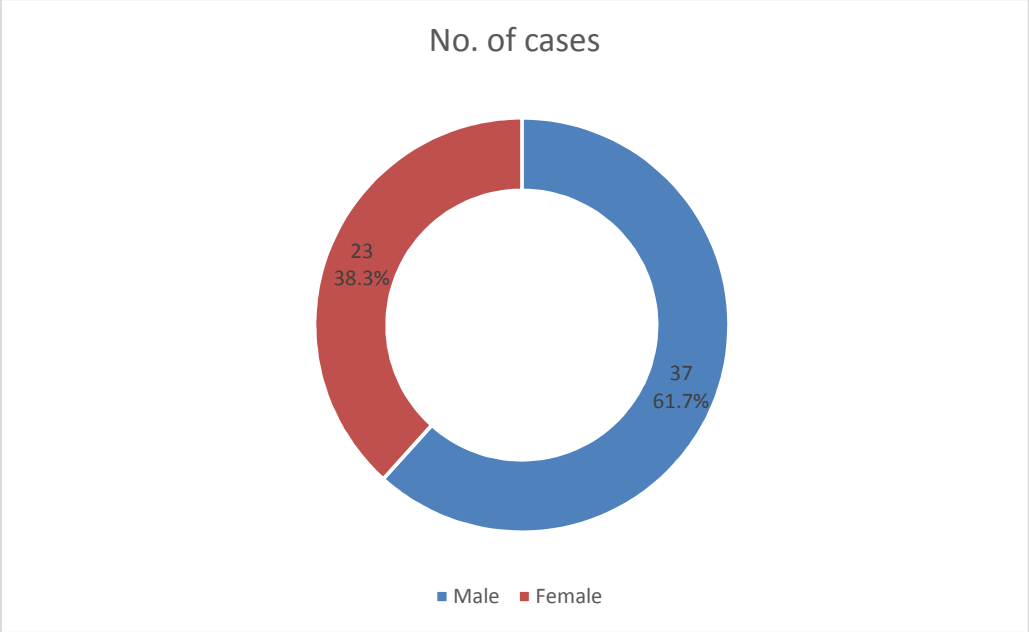


Table 4 :Gravida wise distribution of cases

Gravida	No. of cases	Percentage
Primi	35	58.3
Multi	25	41.6
Total	60	100

Table 4 shows most of the babies were born to primigravida

Graph 4 :Gravida wise distribution of cases

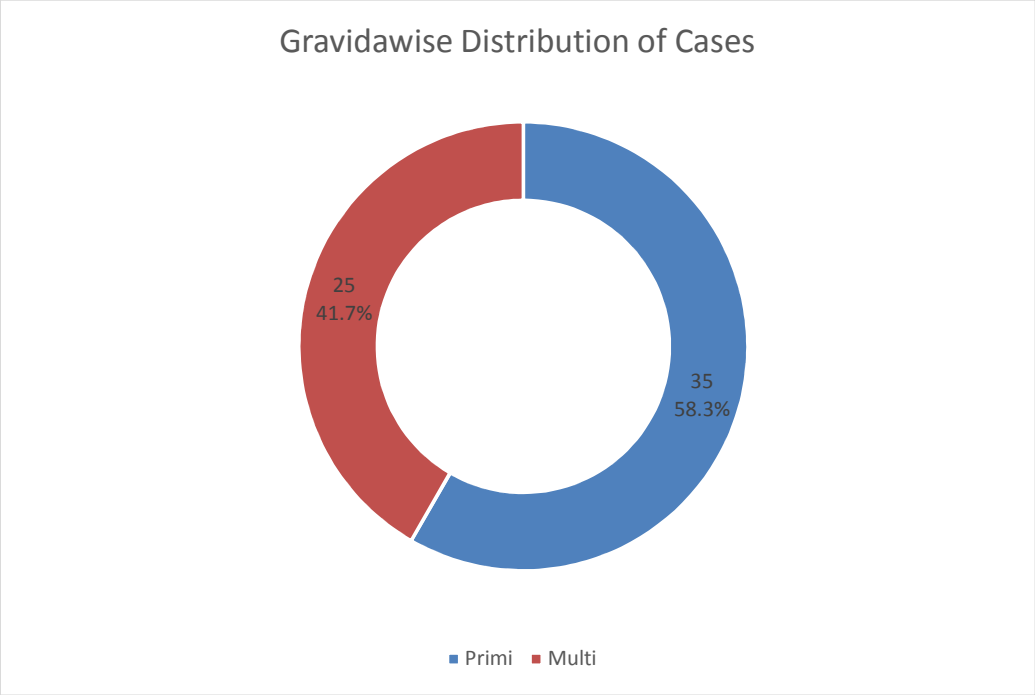


Table 5 : Mode of delivery

Mode of delivery	No. of cases	Percentage
Vaginal	36	60
LSCS	24	40
Total	60	100

Table 5 : Shows majority of babies were born through vaginal route.

Graph 5 : Mode of delivery

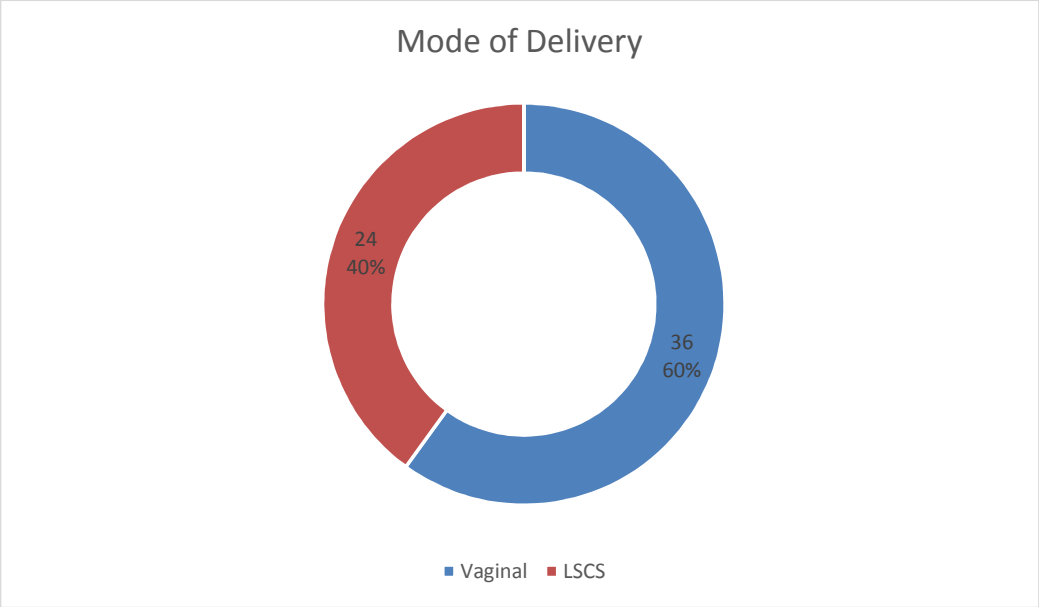


Table 6 : Distribution of cases on the basis of steroid intake

Steroids	No. of cases	Percentage
Received	21	35
Not received	39	65
Total	60	100

Table 6 : Shows 35% of babies had received steroids prenatally.

Graph 6 : Distribution of cases on the basis of steroid intake

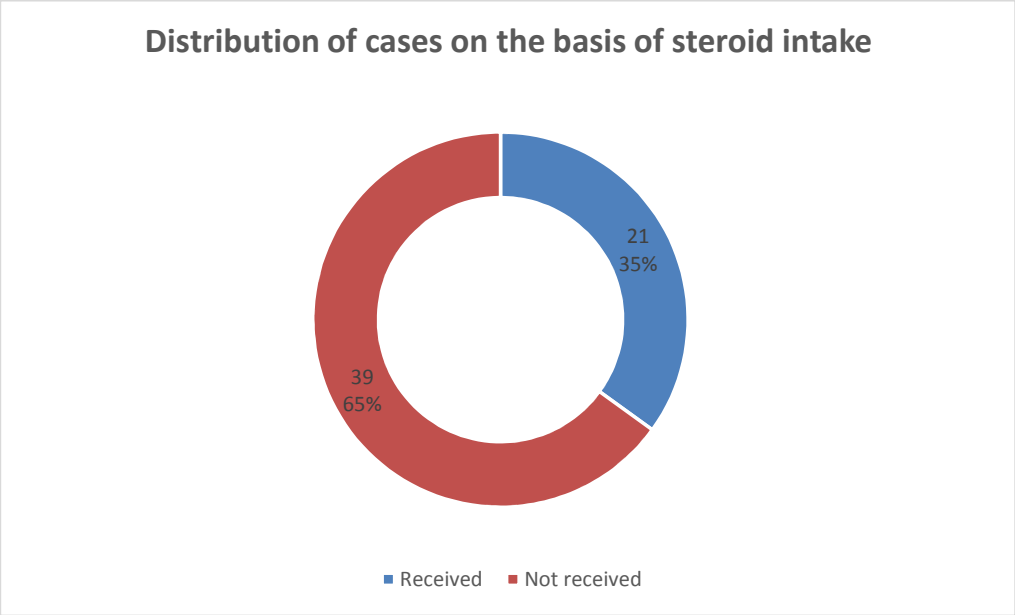


Table 7 : Distribution of various clinical presentations

Clinical presentations	No. of babies	Percentage
Normal	32	53.3
Seizures	6	10
Lethargy	2	3
Absent suckling	2	3
Hydrocephalus	2	3
Excessive cry	3	5
Sudden onset pallor	1	1.6
Respiratory distress	1	1.6
PDA	3	5
Bulging anterior frontanel	1	1.6
Sepsis	1	1.6
Delay cry	6	10
Total	60	100

Table 7 shows majority of babies were presenting with seizures and delay cry

Graph 7 : Distribution of various clinical presentation

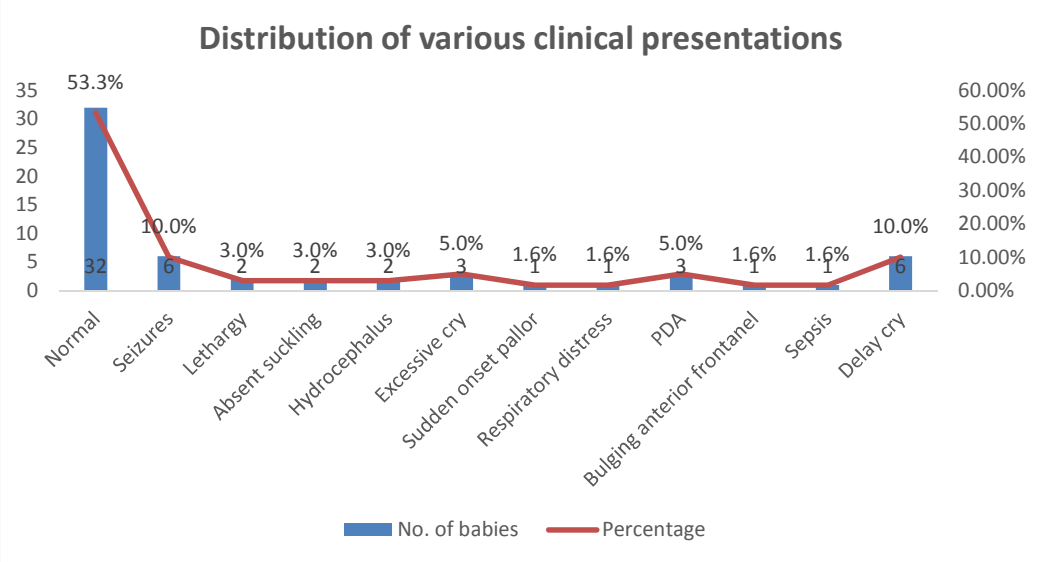


Table 8 : Distribution of brain injuries in gestational age < 32 wks and > 32wks.

Gestational age (wks)	Total No. of babies	No. of babies with brain injuries	Percentage
< 32 wks	32	5	12.3
> 32 wks	28	1	3.5
Total	60	6	

Table 8 shows brain injuries are more in babies born < 32 wks of gestation.

Graph 8 : Distribution of brain injuries in gestational age < 32 wks and > 32 wks.

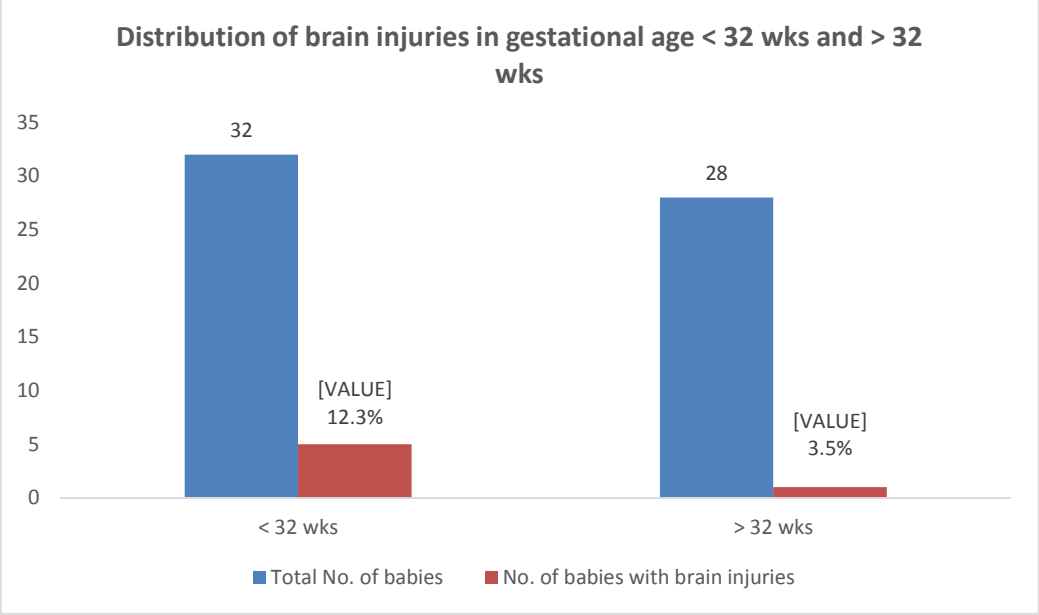


Table 9 : Distribution of brain injuries in birth weight < 1.5 kg and > 1.5 kg.

Birth wt. (kg)	Total No. of babies	No. of babies with brain injuries	Percentage
< 1.5 kg	27	5	18.5
> 1.5 kg	33	1	3
Total	60	6	

Table 9 shows most of the injuries were distributed in babies with birth weight less than 1.5 kg.

Graph 9 : Distribution of brain injuries in birth weight < 1.5 kg and > 1.5 kg.

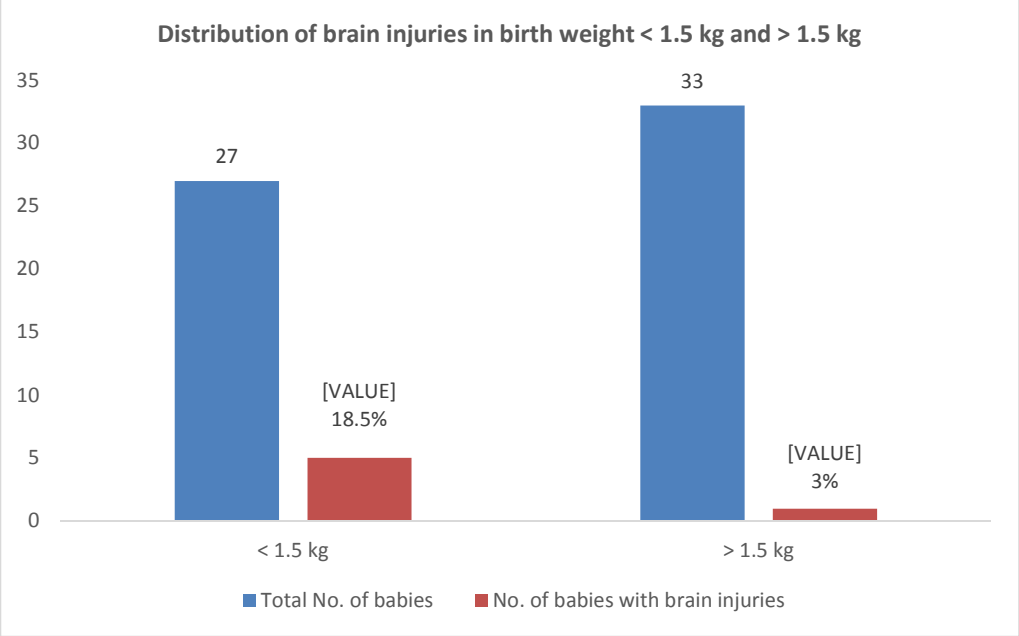


Table 10 : Distribution of brain injuries in babies who have received and not received steroids prenatally.

Steroids	Total No. of babies	No. of babies with abnormal clinical features	Percentage
Received	21	10	47.6
Not received	39	18	46.1
Total	60	28	

Table 10 shows majority of brain injuries were found in babies who had not received prenatal steroids.

Graph 10 : Distribution of brain injuries in babies who have received and not received steroids prenatally.

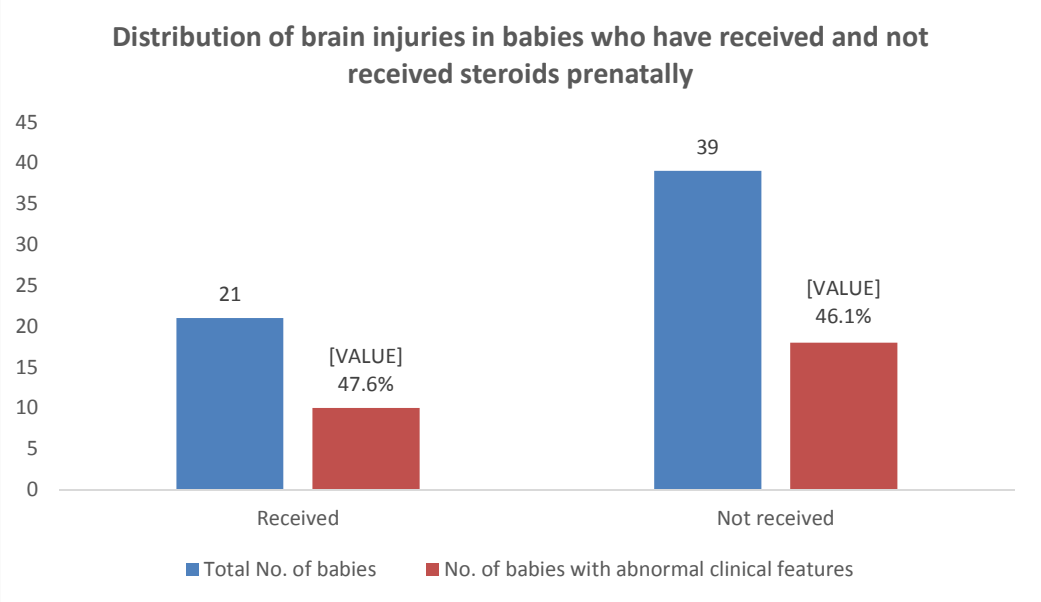


Table 11: Test of significance between average Ri of prematures with steroid & without Steroid

Steroid	ACA Ri:Mean±SD	Z-Value & P-value
Yes	**0.602±0.212**	**Z=1.2 &P≤0.20**
No	**0.564±0.153**	**Conclusion: NSS**

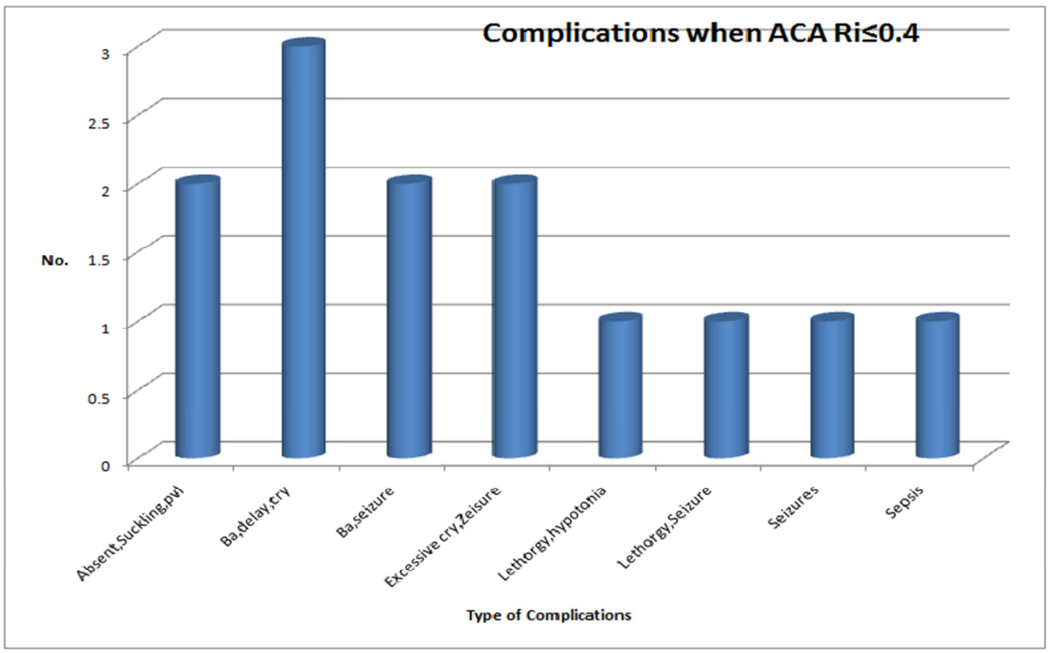
Note: **Steroid could seems to have increased Ri by 15%.**

Table 12 : Table of complications at different levels of ACA RI

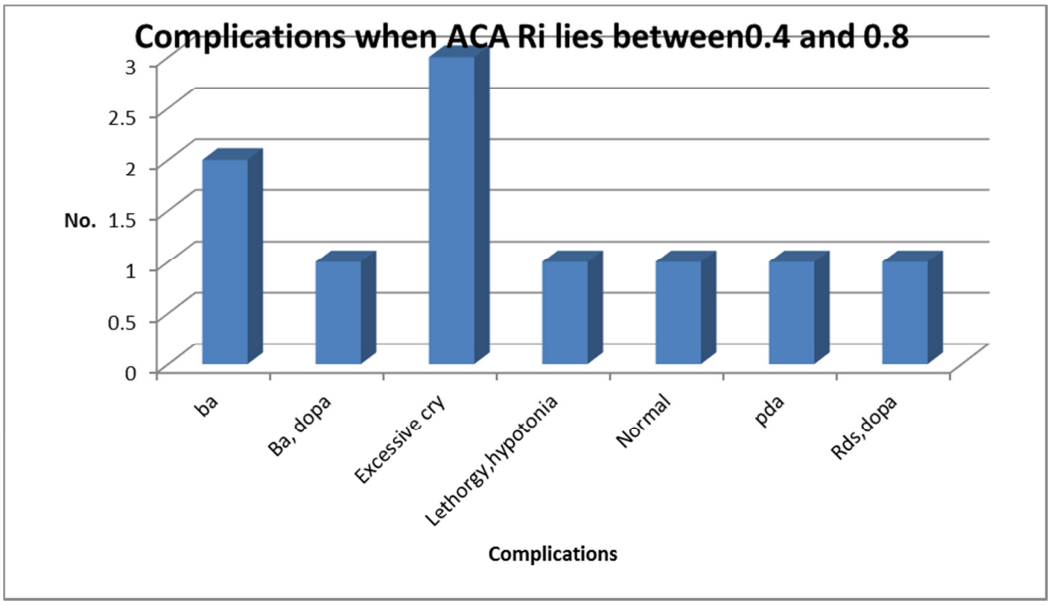
ACA Ri≤0.4		**0.4< ACA Ri>0.8**		**ACA Ri≥0.8**	
Complications	No.=16	Complications	No.=38	Complications	No.=6
Absent, Suckling, pvl	2	Ba	2		1
Ba, delay, cry	3	Ba, dopa	1	Hydrocephalus	1
Ba, seizure	2	Excessive cry	3	Hydrocephalus, dopa	1
Excessive cry, Seizure	2	Lethargy, hypotonia	1	pda	2
Lethargy, hypotonia	1	Normal	1	Sudden onset of pollar,ivh	1
Lethargy, Seizure	1	pda	1	--	--
Seizures	1	Rds,dopa	1	---	---
Sepsis	1	……	….	---	---
Risk Rate:13/16=81.25 %	**13**	**Risk Rate:10/38=26.3%**	**10**	**Risk Rate:6/6=100%**	

Table 11 : Table of complications at different levels of ACA RI shows a relative risk of 81.25% when RI <0.4 and a relative risk of 100% when RI >0.8

Graph 11 : Complications when ACA RI ≤ 0.4



Graph 12 : Complications when ACA RI lies between 0.4 and 0.8



Graph 13 : Complications when ACA RI ≥ 0.8

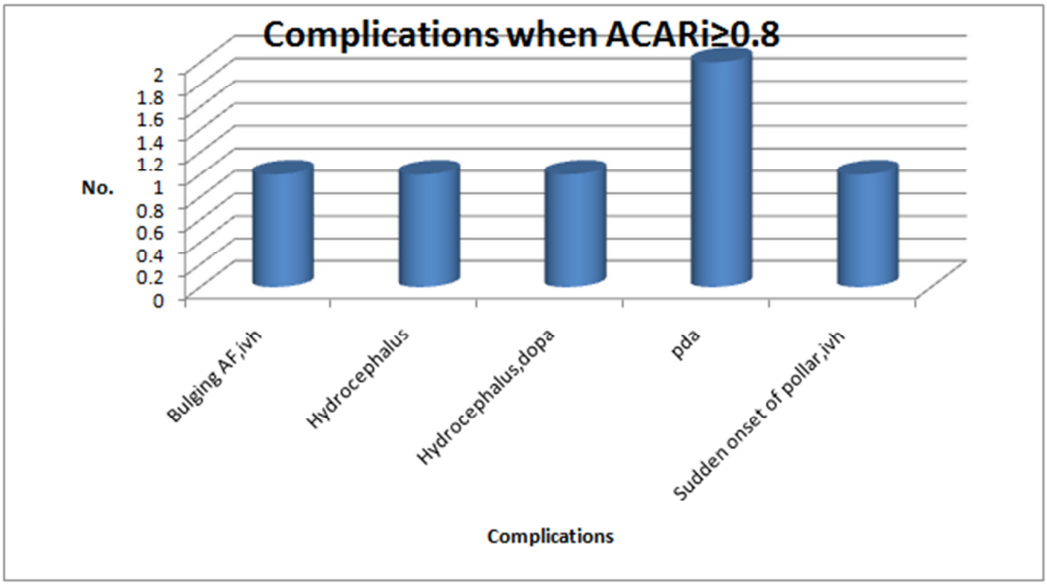


Table 13: Test of Significance for association between Complications and levels of ACA RI

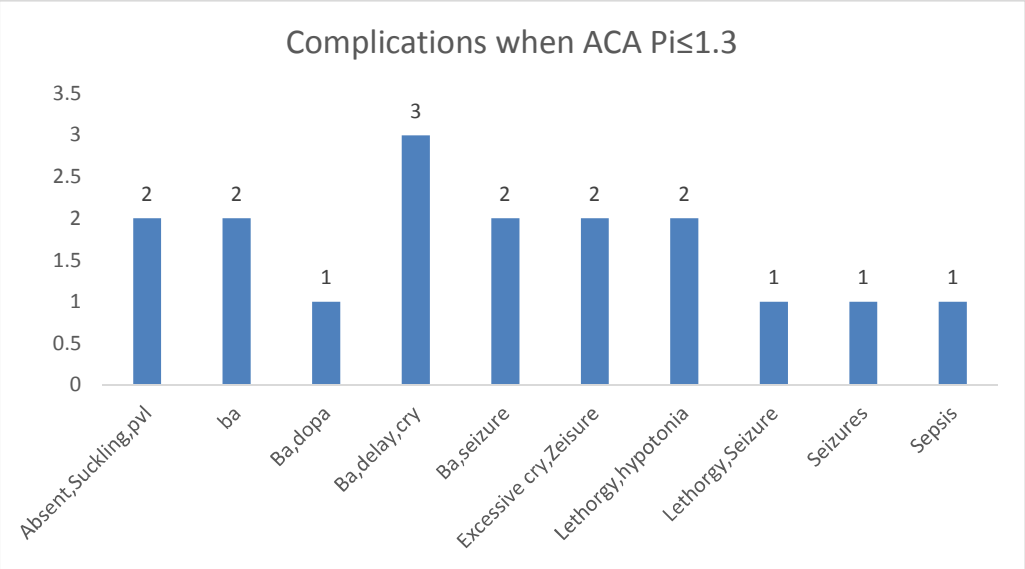
	With Complications	Without Complications	Total
ACA Ri≤0.4	13	3	16
0.4<ACA Ri>0.8	10	28	38
ACA Ri≥0.8	6	0	6
Total	29	31	60

Conclusion: Chi Square test indicates that there is an association between Complications and levels of ACA Ri because the calculated value of Chi-Square is 9.46 which is much greater than table value of Chi-Square (6.64) at one degree of freedom with P-valueless than 0.01

Table 14 : Complications at different levels of ACA Pi.

ACA Pi ≤1.3		**1.3 < ACA Pi >2.5**		**ACA Pi ≥ 2.5**	
Complications	No.=37	Complications	No.=23	Complications	No.=0
Absent, Suckling, pvl	2	pda	3		
Ba	2	normal	1		
Ba,dopa	1				
Ba,delaycry	3	Bulging, AF, ivh	1		
Ba,seizure	2	Excessive cry	2		
Excessive cry, Seizure	2	hydrocephalus	1		
Lethargy, hypotonia	2	Sudden onset pallor, ivh	1		
Lethargy, Seizure	1	Hydrocephalus, dopa	1	--	--
Seizures	1	Rds,dopa	1	---	---
Sepsis	1	……	……	---	---
Risk Rate:17/37=45.9%	**17**	**Risk Rate:11/23=47.8 %**	**11**		

Graph 14 : Complications when ACA PI ≤1.3



Graph 15 : Complications when ACA PI lies between 1.3 and 2.5

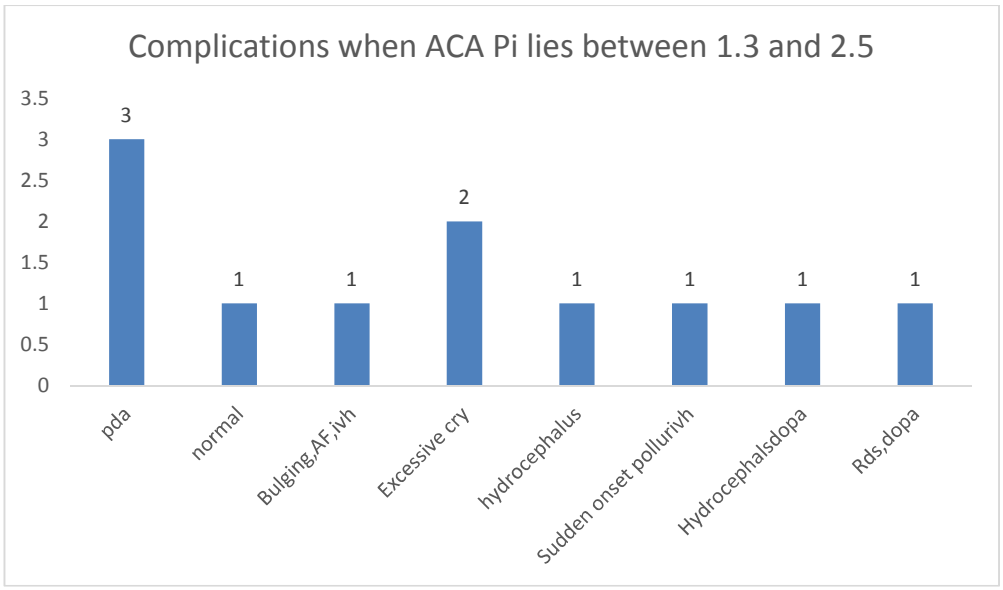
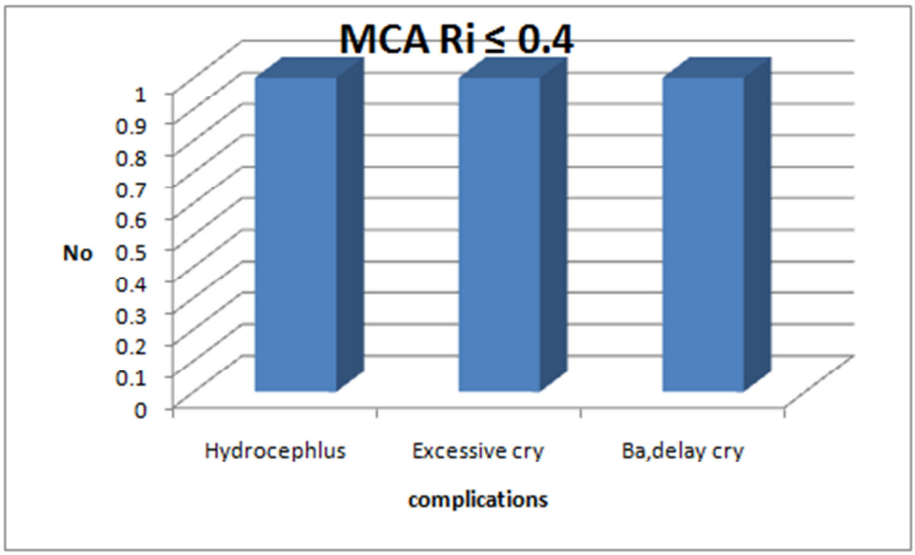


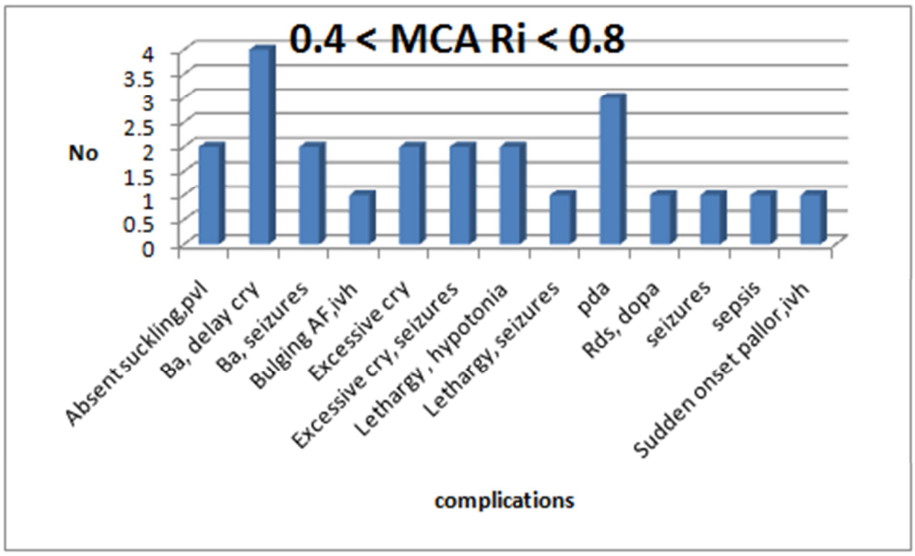
Table 15: Table of Complications at different levels of MCA RI

MCA Ri≤0.4		**0.4< MCA Ri>0.8**		**MCA Ri≥0.8**	
Complications	No.=8	Complications	No.=48	Complications	No.=4
Hydrocephlus	1	Absent suckling,pvl	2	Ba, dopa	1
Excessive cry	1	Ba, delay cry	4	Hydrocephalus, dopa	1
Ba,delay cry	1	Ba, seizures	2		
		Bulging AF,ivh	1		
		Excessive cry	2		
		Excessive cry, seizures	2		
		Lethargy , hypotonia	2		
		Lethargy, seizures	1		
		pda	3		
		Rds, dopa	1		
		seizures	1		
		sepsis	1		
		Sudden onset pallor, ivh	1		
Risk Rate:3/8=37.5 %	**3**	**Risk Rate:23/48=47.9 %**	**23**	**Risk Rate:2/4=50%**	**2**

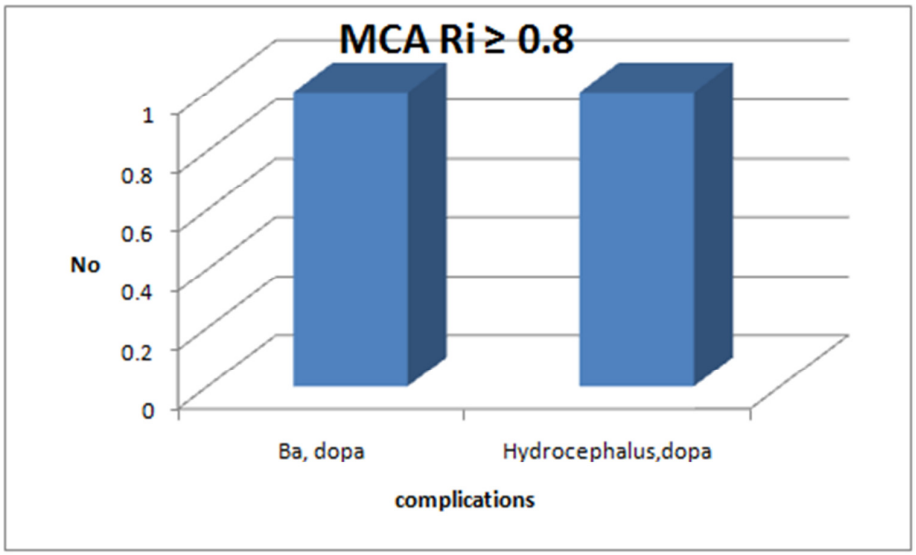
Graph 16 : Complications when MCA RI ≤ 0.4



Graph 17 : Complications when MCA RI is between 0.4 and 0.8

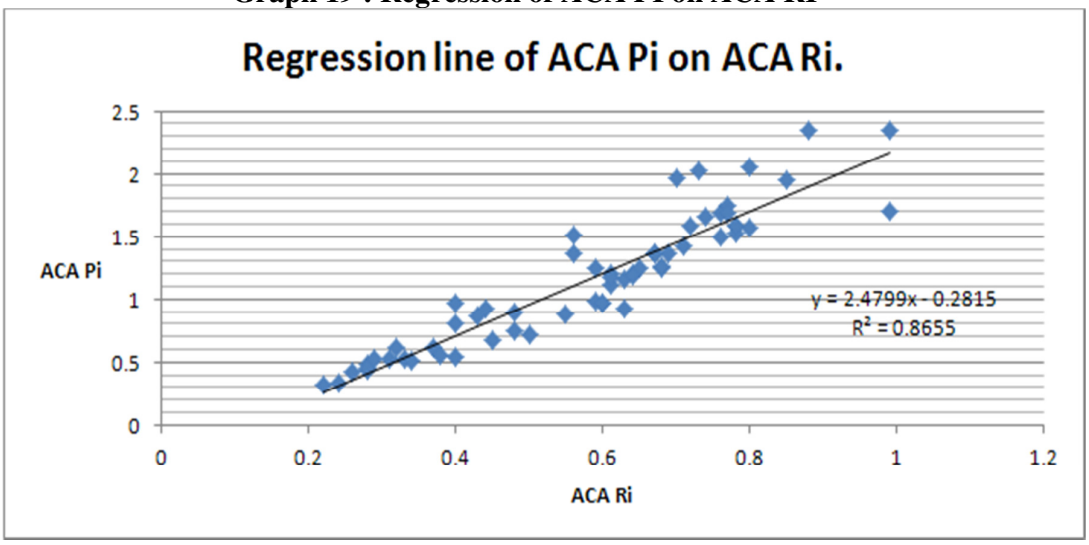


Graph 18 : Complications when MCA RI ≥ 0.8



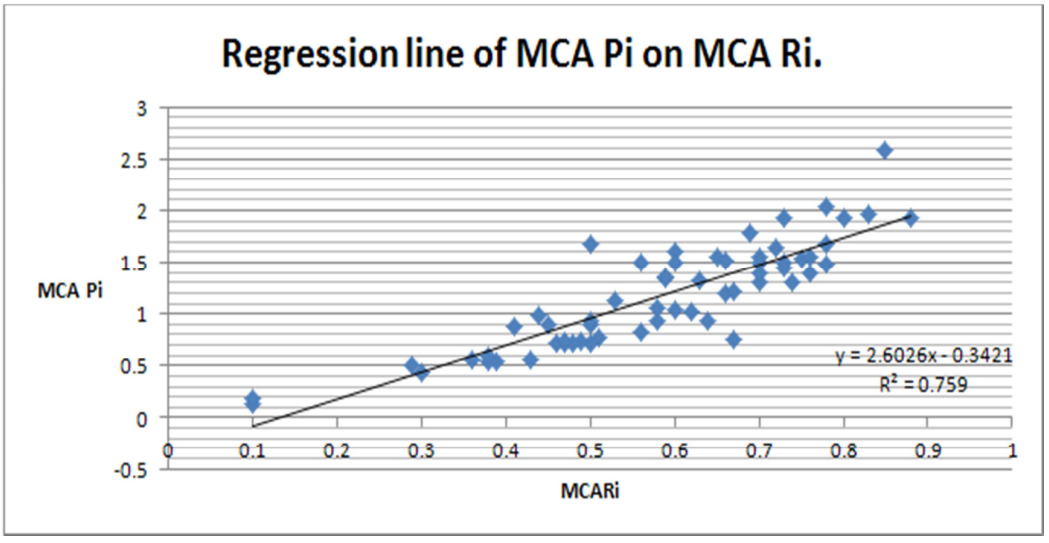
Conclusion: Chi Square test indicates that there is no association between Complications and levels of MCA Ri because the calculated value of Chi-Square is 0.31 which is less than table value of Chi-Square (0.46) at one degree of freedom with P-value less than 0.6

Graph 19 : Regression of ACA PI on ACA RI



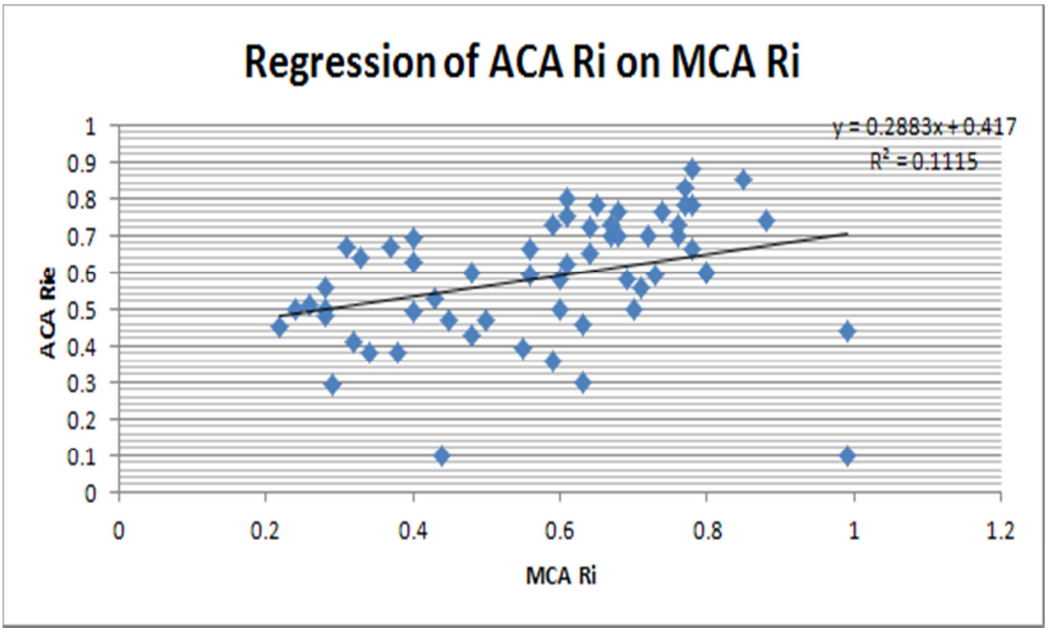
Note: Correlation between ACA Ri and ACA Pi is 0.93 and it is Significant

Graph 20 : Regression of MCA PI on MCA RI



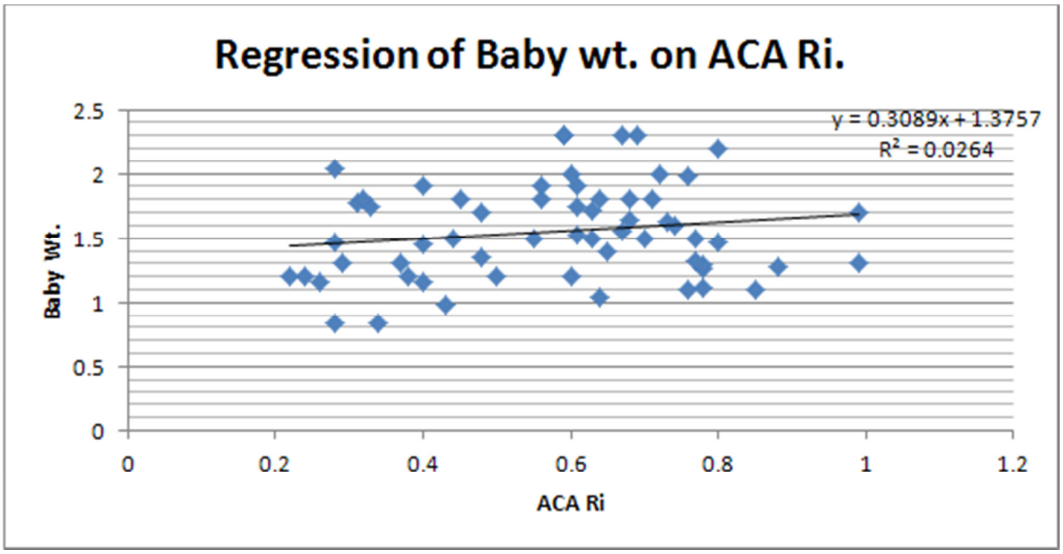
Note: Correlation between MCA Pi and MCA Ri is 0.87 which is Significant.

Graph 21 : Regression line of ACA RI on MCA RI



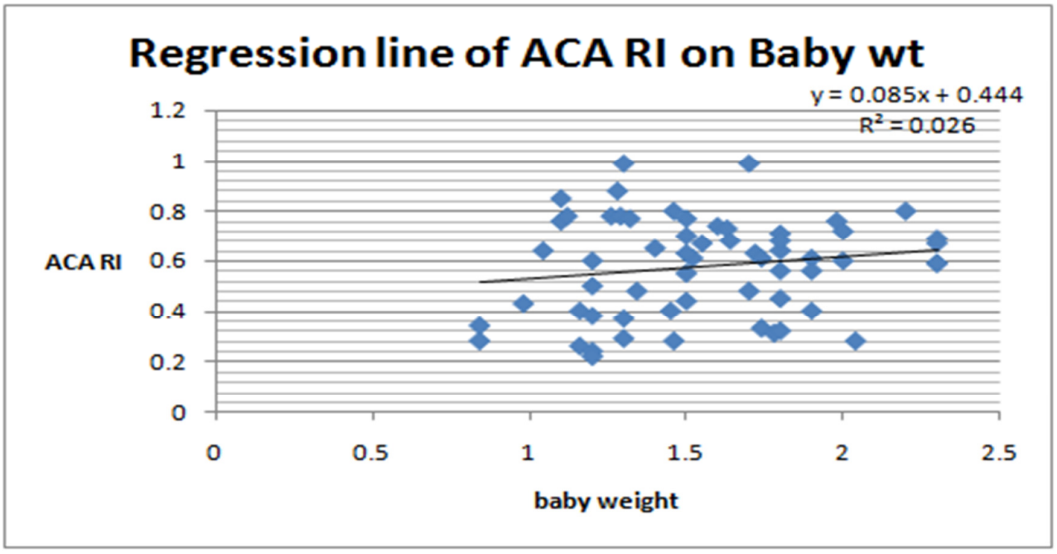
Note: Correlation is +ve but in significant

Graph 22 : Regression of Baby weight on ACA RI



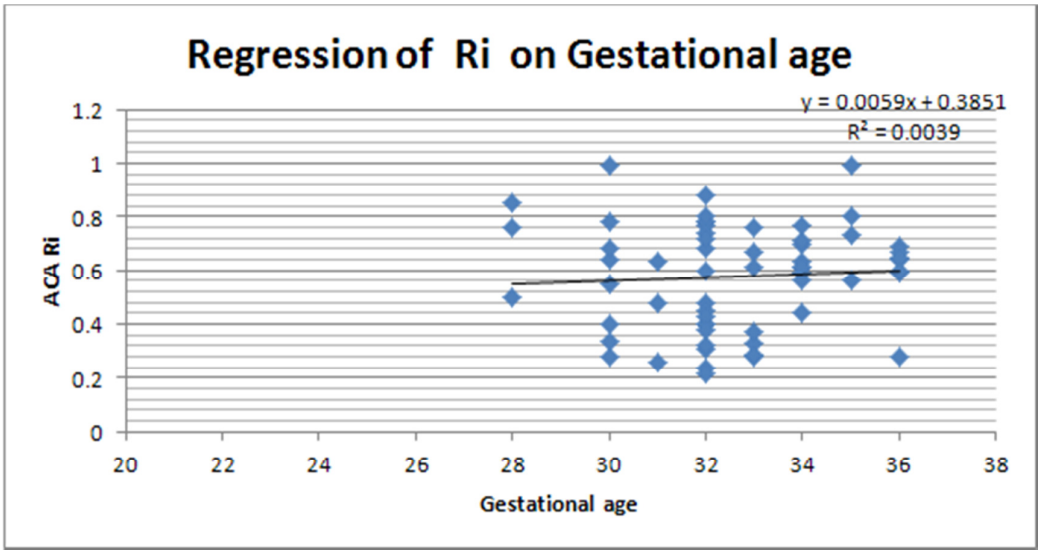
Note: Correlation is 0.1625 though it is +ve but insignificant.

Graph 23 : Regression line of ACA RI on Baby weight



Note: Correlation is 0.1625 though it is +ve but insignificant.

Graph 24 : Regression of RI on Gestational age



Note: Correlation between Gestational Age and ACA Ri is 0.0.06 which is insignificant.

DISCUSSION

The use of ultrasound for transfontanel diagnosis of neurological disorders in neonates is already established due to its sensitivity and specificity in detecting diseases. The use of Doppler technique has enabled us to study the extent of blood flow velocity in cerebral arteries. Neurosonography has now been routinely performed in premature infants. This has produced wealth of information about the central nervous system like GMH, PVL and ventriculomegaly. This information has included timing and evolution of these lesions and their eventual correlation with outcome.

Our study comprised of 60 preterm neonates of suspected brain injuries. The study group had male predominance (61.6%), majority of babies were born to primiparous women (58.3%) and 60% of babies in our study were born through vaginal route.

Study group comprise of babies born between the gestational age of 28 to 36 wks of which majority of them were between 32-34 wks of gestation comprising about 40%. Birth weight was ranging from 1.3 to 2.5 kg of which most babies were between <1.5 kg (45%).

In our study 32 babies were less than 32 wks and 28 babies were more than 32 wks gestational age. Out of 32 babies born less than 32 wks 5 showed abnormal neurosonogram findings i.e., 12.3%. Out of 28 babies > 32 wks gestational age 1 baby showed abnormalities (i.e., 3.5%).

Out of 27 babies weighing < 1.5 kg, 5 babies showed abnormalities forming 18.5% and 33 babies weighing > 1.5 kg, 1 baby showed abnormality forming 3%.

Abnormal neurosonogram findings in babies who have not received steroids were 18 (about 46.1%).

The commonest clinical manifestation in preterm babies in our study was seizures (10%) and delayed cry (10%).

Neurosonogram study performed within 3 days of birth showed abnormal neurosonogram findings in 6 babies and rest of the 54 babies showed normal neurosonogram study.

The deterioration in autoregulation of cerebral blood flow is believed to play a central role in the pathogenesis of intracranial hemorrhages and hypoxic-ischemic lesions.(Levene et al. 1987, 1989; Bel et al. 1993; Ball et al. 1994; Mires et al. 1994; Penning et al. 1994; Krampl et al.994; Krampl et al.2001)

The most common abnormality found on neurosonogram was germinal- matrix haemorrahge, hydrocephalus, periventricular leukomalacia comprising 3% of cases each.

Our study showed periventricular leukomalacia in 2 babies (i.e., 3%) of 60 babies on whom neurosonogram was done. This finding was in common with study done by Rezaie P et al.[20]

From the works of Bada et al. and Pourcelot et al. know that RI can be considered as a relative measure of blood flow velocity and an indicator of vascular resistance. And that elevated RI correlates with vasoconstriction and low blood flow velocity, wheras low RI values correlate with high vasodilation and blood flow velocity.

In our study out of the 14 babies who suffered perinatal asphyxia 10 cases had low RI. Archer et al. study showed that infants after perinatal asphyxia showed low values of RI, PI velocities and high CBF velocities, and that all abnormal values were observed before 72 hours of life. Our results were matching with archer et al., conclusions.

In our study of the 2 babies with IVH and 2 babies with hydrocephalus, it was found that all the babies had increased RI. According to Volpe 1995 decreased CBFV and increased RI are considered diagnostic of post-haemorrhagic hydrocephalus.

The worse outcome occurred among those with a high RI, since all patients had an adverse outcome on the ultrasound examination.

To assess the presence of association between levels of ACA RI and complications Chi-square test was used and found that there is an association. However the test reflected that there is no association between MCA RI and complications. Therefore in the present study it was seen that the Doppler indices obtained from the ACA was more explanatory of the complications than MCA.

Correlation of the Doppler variables PI and RI of ACA were studied through Regression of ACA PI on ACA RI. It was found they were correlated which implies that ACA PI can also be used to evaluate for the neurological outcome of the babies including complications.

To test the significance of the difference between RI levels with steroid and without steroid, the Z statistic was used, and found that there is no significant difference in RI because of steroid. However it seems that an increase of 15% in RI can be expected. It was seen in this study that majority of brain injuries were found in babies who had not received prenatal steroids.

CONCLUSIONS

In our study 60 pre-term babies from gestational age 28 to 36 weeks were studied with ultrasound through anterior fontanel.

RI can be considered as a relative measure of blood flow velocity and an indicator of vascular resistance. And that elevated RI correlates with vasoconstriction and low blood flow velocity, whereas low RI values correlate with high vasodilatation and blood flow velocity.

Doppler indices like RI and PI can be used to evaluate cerebral artery blood flow patter and correlate with neurological abnormalities.

Anterior cerebral artery Doppler indices showed association with complications than Middle cerebral artery Doppler indices.

Commonest clinical presentation was seizures and delayed cry.

The abnormalities found on neurosonogram in our study were germinal matrix hemorrhage, periventricular leucomlacia and hydrocephalus.

High incidence of brain injuries were detected in babies born less than 32 weeks of gestation, weighing less than 1500 gm and those who had not received pre-natal steroids.

Manifestations of the decrease in CBFV in the post asphyxial cerebral hypoperfusion period and improvement of this condition by medications and treatment would prove to be of crucial importance in terms of preventing neuronal damage. Some authors prescribed medications such as prazosin, which would increase CBF (Volpe 1995).

In the presence of post haemorrhagic hydrocephalus and the clinician must be prepared to decrease ventricular dilation using serial LP ventricular drainage, or drugs that decrease decrease production of CSF.

The establishment of a normative database for cerebral Doppler measurement in infants is important for performing preventive and/or therapeutive stabilization of cerebral circulation in infants.

SUMMARY

Neurosonogram remains the accurate, rapid imaging modality of choice for detecting brain injuries in preterm infant.

This technique is both sensitive and specific for detecting germinal matrix hemorrhage and periventricular leucomalacia.

Neurosonogram helps in satisfactory grading of GMH and PVL which in turn helps in studying the prognosis and possible outcome.

Cranial US facilitates early bedside diagnosis and monitoring of pathologies in a way that is relatively easy and not disturbing and safe for the newborn.

It is a useful modality to perform frequent follow-up scans.

The advantages of neurosonogram includes easy to operate, non invasiveness, lack of ionizing radiation, accuracy, bed side availability for unstable infants, rapid diagnosis, wide availability, cost effectiveness and repeatability.

Cranial Doppler USG is of practical importance in evaluating CBFV

Having found RI values with Doppler method the clinician can confidently reassure patients that their baby has little risk of death or handicap and the necessity to be followed up in the high risk OPD.

BIBLIOGRAPHY

1. Martin JA, Hamilton BE, Ventura SJ, Menacker F, Park MM. Births : final data for 2000. Natl Vital Stat Rep. 2002;50:1-101
2. Back SA, Rivkees SA. Emerging concepts in periventricular white matter injury. SeminPerinatol. 2004 Dec;28(6):405-14.
3. Volpe JJ. Neurological evaluation; hypoxic- ischemic encephalopathy; and intracranial hemorrhage. In : Neurology of the newborn. Third edition. Philadelphia, Pennsylvania, W.B. Saunders Company,.1995. p. 95-463.
4. Rumack CM, Drose JA. Neonatal and infant brain imaging. In: Diagnostic ultrasound. 4th edn. Philadelphia, Elsevier, Mosby; 2011.p.1558-163
5. Leksee L: Echo- encephalography In detection of intracranial complications following head injury. Acta Chir Scand .1956;(110):p301-305.
6. De vlieger M, Ridder HJ. Use of echoencephalography. Neurology. 1959 Apr;9(4):216–223.
7. Creed L, Haber K. Ultrasonic evaluation of the infant head. Crit Rev Diagn Imaging. 1984;21(1):37-84
8. London DA, Carroll BA, Enzmann DR. Sonography of ventnicular size and germinal matrix hemorrhage in premature infants. AJNR 1980;1:p.295-300
9. Bowie JD, Kirks DR, Rosenberg ER, Clair MR, Caudothalamic groove: value in identification of germinal matrix hemorrhage by sonography in preterm neonates. AJR Am J Roentgenol. 1983 Dec;141(6):1317-20.
10. McGuinness GA, Smith WL. Head ultrasound screening in premature neonates weighing more than 1,500 g at birth. Am J Dis Child. 1984 Sep;138(9):817-20.

11. Slabaugh RD, Smith JA, Lemons J, Schreiner R, Macdonald N, Cohen MD. Neonatal intracranial hemorrhage and complicating hydrocephalus. J Clin Ultrasound 1984;12(5):261-266.
12. Rumack CM, Manco-Johnson ML, Manco-Johnson MJ, Koops BL, Hathaway WE, Appareti K, Timing and course of neonatal intracranial hemorrhage using real-time ultrasound. Radiology. 1985 Jan;154(1):101-5
13. Guzzetta F, Shackelford GD, Volpe S, Perlman JM, Volpe JJ. Periventricular Intraparenchymal Echodensities in the Premature Newborn: Critical Determinant of Neurologic Outcome .Pediatrics 1986 dec;78(6):995-1006
14. Kirks D, Rand Bowie JD. Cranial ultrasonography of neonatal periventricular /intraventricular hemorrhage: who, how, why and when? Pediatric Radiology 1986.Volume 16, Number 2, p114-119.
15. Amato M, Howald H, von MuraltG. Incidence of peri- intraventricular hemorrhage in premature neonates weighing more than 1500 g. J Perinat Med. 1987;15(1):91-94.
16. Perlman JM, Rollins N, Burns D, Risser R. Relationship between periventricular intraparenchymalechodensities and germinal matrix- intraventricular hemorrhage in the very low birth weight neonate. Pediatrics. 1993 Feb;91(2):474-80.
17. Boal DK, Watterberg KL, Miles S, Gifford KL.Optimal cost-effective timing of cranial ultrasound screening in low-birth-weight infants. PediatrRadiol. 1995;25(6):425-8.
18. Ment LR, Schneider KC, Ainley MA, Allan WC .Adaptive mechanisms of developing brain. The neuroradiologic assessment of the preterm infant. Clinics in Perinatology 2000, 27(2):303-23.

19. Antoniuk S and da Silva RV. Periventricular and intraventricular hemorrhage in the premature infants. Rev Neurol 2000;31(3):238-43.
20. Rezaie, P and Dean, A . "Periventricular leukomalacia, inflammation and white matter lesions within the developing nervous system". Neuropathology : official journal of the Japanese Society of Neuropathology. 2006 sep; 22 (3): 106–132.
21. Linder N, Haskin O, Levit O, Klinger G, Prince T, Naor N, et al. Risk factors for intraventricular hemorrhage in very low birth weight premature infants: a retrospective case control study. Pediatrics 2003;111:590-595.
22. Perry RN, Bowman ED, Murton LJ, Royl RN, Crespigny DE. Cranial ultrasound screening of preterm and term neonates. Journal of Paediatrics and Child Health 2008 march: 23 (1); 31 – 33.
23. Levene MI, Fenton AC, Evans DH, Archer LN, Shortland DB, Gibson NA. Severe birth asphyxia and abnormal cerebral blood flow velocity. Dev Med Child Neurol 1989; 31:427-34
24. Yoshida-Shuto H, Yasuhara A, Kobayashi Y. Cerebral blood flow velocity and failure of autoregulation in neonates: their relation to outcome of birth asphyxia. Neuropediatrics 1992; 23:241-4
25. Gray PH, Tudehope DI, Masel JP, Burns YR, Mohay HA, O'Callaghan MJ, et al. Perinatal hypoxic-ischemic brain injury: prediction of outcome. Dev Med Child Neurol 1993;35:965-73
26. Van Bel F, Van de Bor M, Stijnen T, Baan J, Ruy JH. Aetiological role of cerebral blood flow alterations in development extension of peri-intraventricularhaemorrhage. Dev Med Child Neurol 1987;29:601-14.
27. Argollon N, Lessa I, Ribeiro. Cranial Doppler resistance index measurement in preterm newborns with cerebral white matter lesions. Jornal de pediatria

2006;82(3):221-226.

28. Sadler TW. Langman's Medical Embryology. 7th edn, USA : Williams and Wilkins 1995:374.
29. Osborn AG. Diagnostic neuroradiology. USA. Mosby-year book, : 1994. 1-10.
30. Gerard NJ, Raubaud CA. Invivo MRI with fetal brain cellular migration, J Comp Asst Tomography. 1992;16:265-267.
31. Snell RS. Clinical neuroanatomy : for medical students. 5th edn. Baltimore, USA; Lippincott Williams and Wilkins, 2001.
32. Cremin BJ, Childton SJ, Peacock WJ. Anatomical landmarks in anterior fontanelleultrasonogrpahy; The Br J Radiol 1988;56:517-526.
33. Sanders RC, Winter T. Clinical sonography. A practical guide. 4th edn, USA : Lippincott Williams & Wilkins. 2007;347-348.
34. Chalak LF, Tarumi T, Zhang R. 2014a. The "neurovascular unit approach" to evaluate mechanisms of dysfunctional autoregulation in asphyxiated newborns in the era of hypothermia. Early Hum Dev 90:687-694.
35. Volpe JJ. (ed). 2008. Neurology of the Newborn (5th Ed), Saunders, Philadelphia, USA.
36. Udomphorn Y, Armstead WM, Vavilala MS. 2008. Cerebral blood flow and autoregulation after pediatric traumatic brain injury. PediatrNeurol 38:225-234.
37. Greisen G. 2005. Autoregulation of cerebral blood flow in newborn babies. Early Hum Dev 81:423-428.
38. Liem KD, Greisen G. 2010. Monitoring of cerebral haemodynamics in newborn infants. Early Hum Dev 86:155-158.

39. Tasker RC. 2013. Brain vascular and hydrodynamic physiology. Sem in PediatrSurg 22:168-173.

40. Tyszczuk L, Meek J, Elwell C, Wytt JS. 1998. Cerebral blood flow is independent of mean arterial pressure in preterm infants undergoing intensive care. Pediatrics 102:337-341.

41. Soul JS, Hammer PE, Tsuji M, Saul PP, Bassan H, Limperopoulus C, Disalvo DN, Moore M, Akins P, Ringer S, et al. 2007. Fluctuating pressure-passitivity is common in the cerebral circulation of sick premature infants. Pediatr Res 61:467-473.

42. Khwaja O, Volpe JJ. 2008. Pathogenesis of cerebral white matter injury of prematurity. Arch Dis Child Fetal Neonatal Ed 93:F153-F161.

43. Ballabh P. 2014. Pathogenesis and prevention of intraventricular hemorrhage. ClinPerinatol 41:47-67.

44. Archer L, Levene M, Evans D. 1986. Cerebral artery Doppler ultrasonography for prediction of outcome after perinatal asphyxia. Lancet 15:1116-1118.

45. Pryds O, Greisen G, Lou H, Friis -Hansen B. 1990a. Vasoparalysis associated with brain damage in asphyxiated term infants. J Pediatr 117:119-125.

46. Boylan G, Young K, Panerai R, Rennie JM, Evans DH. 2000. Dynamic cerebral autoregulation in sick newborn infants. Pediatr Res 48:12-17.

47. Vutskits L. 2014. Cerebral blood flow in the neonate. Pediatr Anesthesia 24: 22-29.

48. Greisen G, Munck H, Lou H. 1987. Severe hypocarbia in preterm infants and neurodevelopmental deficit. Acta Paediatr Scand 76:401-4.

49. Okumura A, Hayakawa F, Kato T, Itomi K, Maruyama K, Ishihara N, Kubota T, Suzuki M, Sato Y, Kuno K, et al. 2001. Hypocarbia in preterm infants with

periventricular leukomalacia: The relation between hypocarbia and mechanical ventilation. Pediatrics 107:469-75.

50. Shankaran S, Langer JC, Kazzi SN, Laptook AR, Walsh M. 2006. Cumulative index of exposure to hypocarbia and hyperoxia as risk factors for periventricular leukomalacia in low birth weight infants. Pediatrics 118:1654-9.
51. Collins MP, Lorenz JM, Jetton JR, Paneth N. 2001. Hypocapnia and other ventilation-related risk factors for cerebral palsy in low birth weight infants. Pediatr Res 50:712-719.
52. Pappas A, Shankaran S, Laptook AR, Langer JC, Bara R, Ehrenkranz RA, Goldberg RN, Das A, Higgins RD, Tyson JE, et al. 2011. Hypocarbia and adverse outcome in neonatal hypoxic-ischemic encephalopathy. J Pediatr 158:752-758.
53. Weissman A, Olanovski I, Weiner Z, Blazer S. 2012. Doppler middle cerebral artery peak systolic velocity for diagnosis of neonatal anemia. J Ultrasound Med 31:1381-1385.
54. Liem KD, Hopman JC, Osesburg B, de Haan AF, Kollee LA. 1997. The effect of blood transfusion and haemodilution on cerebral oxygenation and haemodynamics in newborn infants investigated by near infrared spectroscopy. Eur J Pediatr 156:305-310.
55. Pryds O, Christensen NJ, Friis-Hansen HB. 1990b. Increased cerebral blood flow and plasma epinephrine in hypoglychemic, preterm neonates. Pediatrics 85:172-176.
56. Brew N, Walker D, Wong FY. 2014. Cerebral vascular regulation and brain injury in preterm infants. Am J Physiol Regul Integr Comp Physiol 306:R773-R786.
57. Greisen G, Hellström-Westas L, Lou H, Rosen I, Svenningsen N. 1985. Sleep-waking shifts and cerebral blood flow in stable preterm infants. Pediatr Res 19:1156-1159.

58. Perlman JM, Hersovitch P, Kreusser KL, Raichle ME, Volpe JJ. 1985. Positron emission tomography in the newborn: Effect of seizure on regional cerebral blood flow in an asphyxiated infant. Neurology 35:244-247.

59. Barkovich AJ (ed). Brain and spine injuries in infancy and childhood. pediatric neuroimaging. 4thedn. Philadelphia, Lippincots Williams and Wilkins, 2005:207-225.

60. Beck S, Wojdyla D, Say L, Betran AP, Merialdi M, Requejo JH et al. The world wide incidence of preterm birth. Bulletin of the World Health Organization. 2010;88:31-38.

61. Singh U, Singh N and Shikha S. A prospective analysis of etiology and outcome of preterm labour. The journal of Obstetrics and Gynaecology of India. 2007;57(1):48.

62. DeReuck JL. Cerebral angioarchitecture and perinatal brain lesions in premature and full term infants. ActaNeurolScand 1984;70:391-395.

63. Burstein J, Papile LA, Burstein R. Intraventricular hemorrhage and hydrocephalus in premature newborns : a prospective study with CT. Am J Roentgenol 1979;132:631-635.

64. Rumack CM, Manco-Johnson ML, Manco-Johnson MJ. Timing and course of neonatal intracranial hemorrhage using real-time ultrasound. Radiology 1985;154:101-105.

65. Boal DK, Watterberg KL, Miles S, Gifford KL. Optimal cost-effective timing of cranial ultrasound screening in low-birth weight infants. Pediatr Radiology 1995;25:425-428.

66. Govaert P, DeVries LS. An atlas of neonatal brain sonography. 2ndedition, UK, Mac Keith Press; 2010, p-199-224.

67. Govaert P, de Vries LS (ed). 2001. An Atlas of Neonatal Brain Sonography, Mac Keith Press, London, UK.

68. Purkayastha S, Sorond F. 2012. Transcranial Doppler ultrasound: Technique and Application. Semin Neurol 32:411-420.

69. Stuart B, Drumm J, Fitzgerald DE, Duignan NM. 1980. Fetal blood velocity waveforms in neonatal pregnancy. Br J ObstetGynaecol 87:780-785.

70. Gosling RG, Dunbar G, King DH, Newman DL, Side CD, Woodcock JP, Fitzgerald DE, Keates JS, MacMillan D. 1971. The quantitative analysis of occlusive peripheral arterial disease by a non-instrusive technique. Angiology 22:52-55.

71. Pourcelot L. 1975. Application clinique de l'examen Doppler trancutane: In: Peronneau P, ed. VelocimetreUltrasonore Doppler. Paris: Inserm. 213-240.

72. Greisen G, Johansen K, Ellison PH, Fredrikson PS, Mali J, Friis-Hansen B. 1984. Cerebral blood flow in the newborn infant: comparison of ultrasound and Xenon-133 clearance. J Pediatr 104:411-418.

73. Lowe LH, Bailey Z. 2011. State-of-the-Art Cranial Sonography: Part I, Modern Techniques and Image Interpretation. AJR 196:1028-1033.

74. Bada HS, Haijar W, Chua C, Sumner DS. 1979. Noninvasive diagnosis of neonatal asphyxia and intraventricular hemorrhage by Doppler ultrasound. J Pediatr 95:775-9.

75. Gray PH, Griffin EA, Drumm JE, Fitzgerald DE, Duigan NM. 1983. Continuous wave Doppler ultrasound in evaluation of cerebral blood flow in neonates. Arch Dis Child 58:677-81.

76. Archer LNJ, Evans DH, Levene MI. 1985. Doppler ultrasound examinations of the anterior cerebral arteries of normal newborn infants. the effect of postnatal age. Early Hum Dev 10:255-60.

77. Deeg KH, Rupprecht TH. 1989. Pulsed Doppler sonographic measurement of normal values for the flow velocities in the intracranial arteries for healthy newborns. PediatrRadiol 19:71-8.

78. Cheung YF, Lam PKL, Yeung CY. 1994. Early postnatal cerebral Doppler changes in relation to birth weight. Early Hum Dev 37:57-66.

79. Meek JH, Tyszcuzuk L, Elwell CE, Wyatt JS. 1998. Cerebral blood flow increases over the first three days of life in extremely preterm neonates. Arch Dis Child Fetal Neonatal 78:F33-F37.

80. d'Orey C, Mateus M, Guimaraes H, Ramos I, Melo MJ, Silva J, Ramos E, Montenegro N, Barros H, Santos N. 1999. Neonatal cerebral Doppler: Arterial and venous flow velocity measurements using colour and pulsed Doppler system. J Perinatol Med 27:352-361.

81. Pezzati M, Dani C, Biadaioli R, Filippi L, Biagiotti R, Giani T, Rubaltelli FF. 2002. Early postnatal Doppler assessment of cerebral blood flow velocity in healthy preterm and term infants. Dev Med Child Neurol 44:745-752.

82. Romagnoli C, Giannantonio C, De Carolis MP, Gallini F, Zecca E, Papacci P. 2006. Neonatal color Doppler US study: Normal values of cerebral blood flow velocities in preterm infants in the first month of life. Ultrasound in Med &Biol 32:321-331.

83. Bulas DI. 2009. Transcranial Doppler: Applications in Neonates and Children. Ultrasound Clin 4:533-551.

84. Allison JW, Faddis LA, Kinder DL, Robertson PK, Glasier CM, Seibert JJ. 2000. Intracranial resistive index (RI) values in normal term infants during the first day of life. Pediatr Radiol 30:618-620.

85. Perlman JM, MacMenamin JB, Volpe JJ. 1983. Fluctuating cerebral blood flow velocity in respiratory distress syndrome. N Engl J Med. 309:204-209.

86. Deeg KH, Rupprecht TH, Zeilinger G. 1990. Doppler sonography classification of brain edema in infants. PediatrRadiol 20:509-514.

87. Fukuda S, Kato T, Kakita H, Yamada Y, Hussein MH, Kato I, Suzuki S, Togari H. 2006. Hemodynamics of the cerebral arteries of infants with periventricular leukomalacia. Pediatrics 117:1-8.

88. Perlman JM, Hill A, Volpe JJ. 1981. The effect of patent ductusarteriosus on flow velocity in the anterior cerebral arteries: Ductal steal in the preterm newborn infant. J Pediatr 99:767-771.

89. Kupferschmid C, Lang D, Pohlandt F. 1988. Sensitivity, specificity and predictive value of clinical findings, m-mode echocardiography and continuous-wave Doppler sonography in the diagnosis of symptomatic patent ductusarteriosus in preterm infants. Eur J Pediatr 147:279-82.

90. Chiu NC, Shen YE, Ho CS. 2003. Outcome in children with significantly abnormal cerebral blood flow detected by Doppler ultrasonography: Focus on the survivors. J Neuroimaging 13:53-56.

ANNEXURES

ETHICAL CLEARANCE CERTIFICATE

Institutional Ethical Committee
BIJAPUR-586 103.
OUTWARD
No. 52/13
Date. 14-11-13
B.L.D.E.U's Shri B.M. Patil Medical College.

B.L.D.E. UNIVERSITY'S
SHRI.B.M.PATIL MEDICAL COLLEGE, BIJAPUR-586 103
INSTITUTIONAL ETHICAL COMMITTEE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Ethical Committee of this college met on 13-11-2013 at 3-30pm to scrutinize the Synopsis of Postgraduate Students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected & revised version synopsis of the Thesis has been accorded Ethical Clearance.

Title "Evaluation of cerebral artery blood flow pattern in premature babies & its correlation with neuro-logical abnormalities" - A cross sectional observational study

Name of P.G. student Dr Robin M. Thomas
Department of Pediatrics

Name of Guide/Co-investigator Dr R. H. Gobbur.
Professor of Pediatrics.

DR.TEJASWINI. VALLABHA
CHAIRMAN
INSTITUTIONAL ETHICAL COMMITTEE
BLDEU'S, SHRI.B.M.PATIL
MEDICAL COLLEGE, BIJAPUR.

Following documents were placed before E.C. for Scrutinization
1) Copy of Synopsis/Research project.
2) Copy of informed consent form
3) Any other relevant documents.

BLDEA'S SHRI B.M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE, VIJAYAPUR-586103

RESEARCH INFORMED CONSENT FORM

TITLE OF THE PROJECT: "EVALUATION OF CEREBRAL ARTERY BLOOD FLOW PATTERN IN PREMATURE BABIES AND ITS CORRELATION WITH NEUROLOGICAL ABNORMALITIES, A CROSS SECTIONAL OBSERVATIONAL STUDY"

GUIDE : Dr. R.H.GOBBUR, MD

PROFESSOR

DEPARTMENT OF PAEDIATRICS

PG STUDENT : Dr. ROBIN M THOMAS

PURPOSE OF RESEARCH

I have been informed that the present study will help in determining the prognosis in preterm babies by means of evaluating their cerebral blood flow pattern by cerebral Doppler ultrasonography.

PROCEDURE :

I understand that after having obtained a detailed clinical history, thorough clinical examination and relevant investigations, a final work up and its outcome is planned.

RISK AND DISCOMFORT :

I understand that I may experience some pain and discomfort during the examination or during treatment. This is mainly the result of my condition and the procedures of this study are not expected to exaggerate this feeling which is associated with usual course of treatment.

BENEFITS :

I understand that my participation in the study will have no direct benefit to me other than the potential benefit of the treatment.

CONFIDENTIALITY :

I understand that the medical information produced by this study will become part of hospital records and will be subject to confidentiality. Information of sensitive personal nature will not be part of medical record, but will be stored in the investigations research.

If data is used for publication in medical literature or for teaching purpose no name will be used and other identifiers such as photographs will be used only with special written permission. I understand that I may see the photograph before giving permission.

REQUEST FOR MORE INFORMATION:

I understand that I may ask more questions about study at any time; Dr. Robin M Thomas at the department of pediatrics is available to answer my questions or concerns. I understand that I will be informed of any significant new finding discovered during the course of the study, which might influence my continued participation. A copy of this consent form will be given to me to keep for careful reading.

REFUSAL OR WITHDRAWAL FROM PARTICIPATION :

I understand that my consent is voluntary and that I may refuse to participate or may withdraw consent and discontinue participation in the study at any time without prejudice. I also understand that Dr. Robin M Thomas may terminate my participation in the study after he has explained reasons for doing so.

INJURY STATEMENT:

I understand that in the unlikely event of injury to my baby resulting directly from participation in this study, if such injury was reported promptly, the appropriate treatment would be available. But, no further compensation would be provided by the hospital. I understand that by my agreement to participate in this study and I am not waiving any of my legal rights.

SIGNATURE OF PATIENT / RELATIVE

NAME AND RELATION TO THE PATIENT

I have explained to shri / smt _____the purpose of the research, the procedures required and possible risks to the best of my ability.

_____

Dr . ROBIN M THOMAS(INVESTIGATOR)

DATE

STUDY SUBJECT CONSENT STATEMENT

I confirm that Dr. Robin M Thomas has explained to me the purpose of research and the study procedure. I am willing to allow my baby to undergo the investigation and the possible discomforts as well as benefits. I have been explained all the above in detail in my own language and I understand the same. Therefore I agree to give consent to participate as subject in this research purpose.

_____ _____

PARENTS / GAURDIAN DATE

_____ _____

WITNESS TO SIGNATURE DATE

PROFORMA

SCHEME OF CASE TAKING

1) Baby of (Mother's Name)
2) Sex
3) Date and time of birth
4) Hospital number
5) Date of admission
6) Date of discharge
7) APGAR score
8) Presenting complaints
    a) Seizures
    b) Lethargy
    c) Excessive cry
    d) Sudden onset pallor
    e) Poor suckling/absent suckling
    f) Bulging anterior fontanelle
    g) Flaccidity
    h) Hypotonia
    i) hypertonia
9) Maternal history GPLA
10) Gestational age (in weeks)
11) History of intake of prenatal steroids;

12) Mode of delivery

a) Vaginal delievery

b) Assisted breech

c) Forceps

d) Cessarian

10) Vitals

a) Pulse

b) Respiratory rate

c) Temperature

11) General physical examination

Gestational age :

Length (cm) :

Birth weight :

Head circumference :

12) RS, CVS, P/A (positive if any)

13) CNS examination

i) Anterior fontanelle

a) Normal

b) Bulged

c) Depressed

ii) Level of consciousness

a) Hyperactive

b) Lethargic

c) Stuperous

d) Coma

iii) Tone

a) Normal

b) Hypotonic

c) Flaccid

iv) Any other if positive

15) Investigations (positive if any)

16) Color Doppler result :

Resistive index, RI :

Pulsatality index, PI :

17) Complications and outcome :

KEY TO MASTER CHART

ACA	–	Anterior cerebral artery
AF	–	Anterior fontanelle
BA	–	Birth asphyxia
B/o	–	Baby of
DOL	–	Day of life
Dopa	–	Dopamine
F	–	Female
IVH	–	Inrtraventricular hemorrhage
LSCS	–	Lower segment caesarian section
M	–	Male
MCA	–	Middle cerebral artery
Multi	–	Multigravida
N	–	Normal
PDA	–	Patent ductus arteriosus
Primi	–	Primipara
PI	–	Pulsatality index
PVL	–	Periventricular leukomalacia
RDS	–	Respiratory distress syndrome
RI	–	Resistive index
Sl no	–	Serial no