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CORRELATION OF DIFFERENT PHASES OF CVI IN CHILDREN AGED ONE TO FOUR YEARS WITH MRI: A ONE YEAR CROSS SECTIONAL STUDY.

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"CORRELATION OF DIFFERENT PHASES OF CVI IN CHILDREN AGED ONE TO FOUR YEARS WITH MRI: A ONE YEAR CROSS SECTIONAL STUDY."

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BELAGAVI, KARNATAKA.

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KLE ACADEMY OF HIGHER EDUCATION AND
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LIST OF ABBREVIATIONS

CVI - Cerebral Visual Impairment

CTVI - Certified Teacher of the Visually Impaired

CT - Computed Tomography

MRI - Magnetic Resonance Imaging

LGB- Lateral Geniculate Body

TAC - Teller Acuity Cards

GDD - Global Developmental Delay

CP - Cerebral Palsy

IQ – Intelligence Quotient

NICU – Neonatal Intensive Care Unit

PVL - Periventricular Leukomalacia

HIE – Hypoxic Ischemic Encephalopathy

fMRI - Functional MRI

PET - Positron Emission Tomography

SPECT- Single Photon Emission Computed Tomography

ABSTRACT

BACKGROUND

Aim:
To study the correlation of different phases of Cerebral Visual Impairment (CVI) with MRI scoring in children aged 1-4years.

Objective:
To correlate MRI scoring with different phases of Cerebral Visual Impairment (CVI) in children aged 1-4years.

Methodology:
The present study was a one-year cross-sectional study conducted at a teaching institute in North Karnataka during the period 1st August 2022 to 31st July 2023. Considering the prevalence of Cerebral Visual Impairment (CVI), the sample size calculated was 29. The study population consisted of children aged 1 to 4years diagnosed with CVI without ocular pathologies, attending the Child Developmental Clinic. Visual acuity was assessed using Teller's Acuity Cards. MRI of the brain performed.
The correlation between visual acuity and MRI scoring was analysed in different phases of CVI. The association of different variables with CVI phases and MRI Score were also assessed.

Results:
Most of the children in our study were below 3 years old. The severity and characteristics of CVI can influence visual functioning at different ages. Refractive errors may coexist with CVI. The presence of squint and nystagmus did not vary across different CVI phases. A significant association was noted between MRI Score with vision and CVI phases. MRI score in those with CVI phase I is significantly more as compared to those in CVI phase III. Further we found that there is a significant association of occipital lobe with CVI Phases (when compared among parietal, temporal and occipital lobe)**.** There is significant moderate negative correlation between vision and MRI score.

Conclusion:
Our findings suggest that there is direct correlation MRI and CVI phase. This study contributes to our understanding of the correlation between MRI Score and CVI Phase in children. It emphasizes that CVI is a complex condition involving multiple factors and domains of visual function. Further research and comprehensive assessments are necessary to fully comprehend the visual impairments in CVI.

Key Words: CVI, MRI, HIE, PVL, Visual acuity

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INTRODUCTION:

"Retina is a piece of brain" says Stephen Ryan in Retina.

Vision is a result of complex system of which eyes are an integral part. Up to 40% of the brain is involved in the processing of visual information. The entire process begins with eyes perceiving visual stimuli and terminates in the brain centers which interpret and translate the data into visual images. [1]

Whiting et al. first used the term "Cortical" Visual Impairment in 1985 to characterize visual impairment in children that resulted from injury to early visual cortical regions, of non-ocular pathology. [2,3]It is now clear that injury to white matter pathways, sub-cortical structures, and higher-order associative processing regions of the cortex, in addition to damage to the visual cortex, is frequently linked to cortical vision impairment. Thus, "Cerebral" instead of "cortical" was considered as a more appropriate term.[4]

Cortical visual impairment is brain based visual impairment, often starts in early childhood and is related to distinct visual and behavioral features that cannot be explained by any ocular causes. Damage to the retro geniculate pathway during the early stages of prenatal development is the cause.

Recently it is observed that in developed countries, Cerebral Visual Impairment (CVI) has become the most common cause of visual impairment in children. [5] The survival rate of preterm newborns and neonates with perinatal brain damage is rising in developing nations like India, which is contributing to an increased prevalence of CVI in children.

Matt Tietjen, CTVI and leader in the field explains CVI as,
"The brain has difficulty converting the raw data from the eye into a reliable, meaningful image of the world that can be interpreted and acted upon."

The American Academy of Neurology and the Practice Committee of the Child Neurology Society advise neuroimaging as part of the assessment process in the evaluation of a child with neurological deficit if the etiology has not been established.

Magnetic resonance imaging (MRI) is preferred over computed tomography when it comes to indicating the etiology and time of the injury since the vast majority of children diagnosed with cerebral palsy (CP) and other neurological abnormalities exhibit aberrant neuro-radiological findings.[6,7,8]

It appears that there is a much more complex and still unclear relationship between the clinical behavioral findings in children with CVI and the underlying development of brain structures and function. [6]

There is limited research on brain lesions in children with cerebral visual impairment (CVI) of various etiologies and has not received much attention in the literature.

Furthermore, studies evaluating the correlation between different phases of CVI and MRI scoring are lacking [6,7] especially in Indian scenario where perinatal complications are of a different nature than in western countries.

In children less than one year of age, MRI findings are inconsistent. Hence children aged one to four years are chosen in view of high neuroplasticity where impact of intervention is maximum.

We believe that this study will help overcome the knowledge gap and add to more awareness about CVI. It will help in the early recognition and rehabilitation of these kids.

Late presentation, inability to identify the cause of blindness and neglect among the general population can be avoided if they have a deeper understanding of the cause and they can be made to understand the importance of early intervention

OBJECTIVES:

To study the correlation of different phases of Cerebral Visual Impairment (CVI) in children aged one to four years with MRI that is Radiological Scoring .

REVIEW OF LITERATURE:

History:

The term "cortical visual impairment" was created to distinguish itself from "cortical blindness," a disorder that was initially identified in soldiers during World War I. This condition affected adults with back of the brain gunshot injuries.

Visual image generation is the domain of the occipital lobe, whereas object movement perception is the function of the middle temporal lobe.

The Riddoch Phenomenon, also known as statokinetic dissociation, is the phenomenon wherein individuals with occipital lobe injury, who should not be able to see, can see to a degree, when there is movement. With blindsight, the information from your eyes travels all the way to the brain to an area in the thalamus called the pulvinar which is attributed to the residual functioning M neurons.

Epidemiology:

With the improvement of prenatal care facilities and a rise in preterm infant survival rates, CVI is currently one of the leading cause of visual impairment in developed countries and increasingly common worldwide. [9]

Concomitant causes of visual impairment in children with multiple disabilities may be attributed to primary ocular pathologies, including uncorrected refractive error, nystagmus, retinopathy of prematurity (ROP), cataract, optic nerve atrophy, and delayed visual maturation.

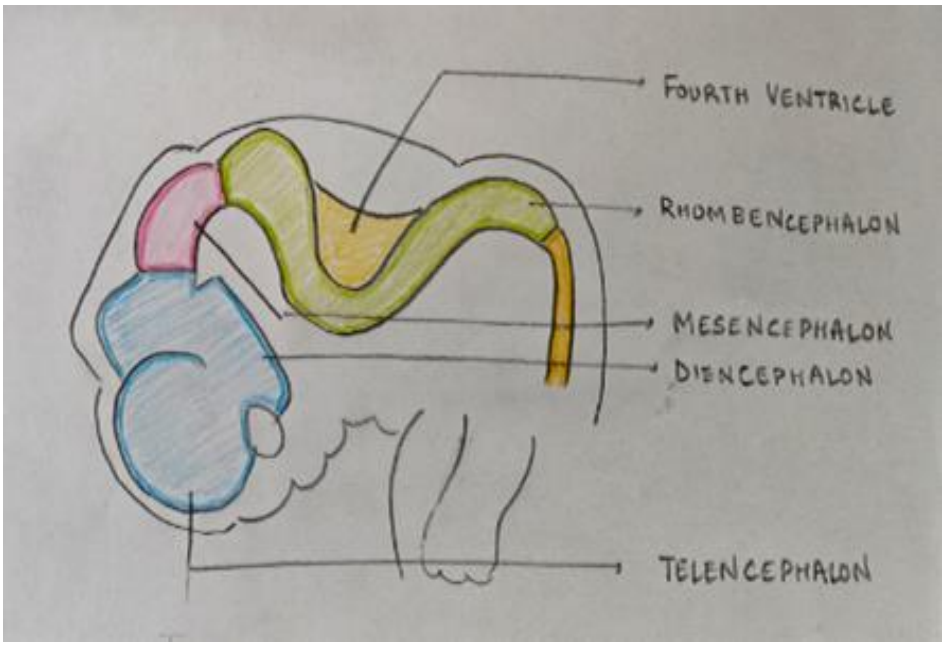
It has been noted that the incidence of CVI increased from 36 per 100,000 in the late 1980s to 161 per 100,000 in 2003. Over the past few decades, there has been a steady increase in the prevalence of CVI in children. [10, 11] Better neonatal intensive care unit facilities have led to a decrease in neonatal mortality, which in turn has contributed to an increase in CVI cases in India. The most common cause of CVI in India is hypoxic ischemic encephalopathy. [12] Other causes include meningitis, hydrocephalus, and retinopathy of prematurity.

Development of brain

Neural system is one of the first systems to start and the last to finish developing after birth.
The expanded cranial portion of the neural tube gives rise to the brain. At about 4th week of gestation, the enlarged cephalic part shows three dilations i.e, the primary brain vesicles craniocaudally these are:

i) Prosencephalon
ii) Mesencephalon
iii) Rhombencephalon

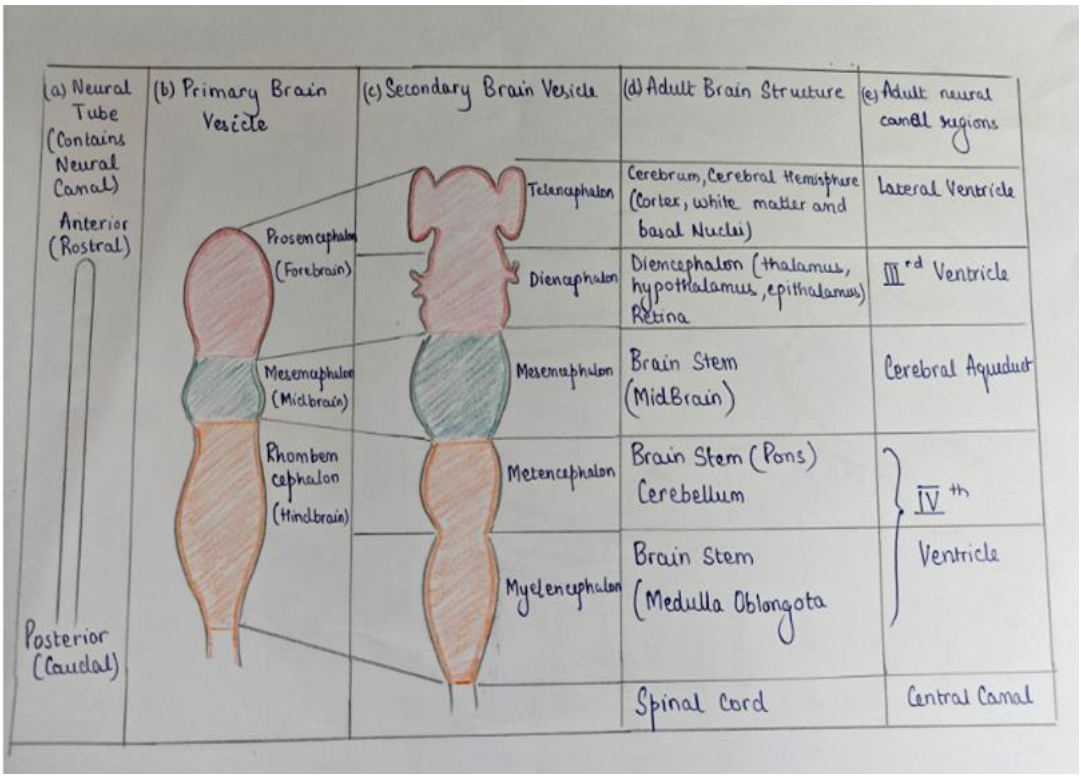
Figure 1:



Brain Damage can result from insult occurring during the development of brain at various stages. The following are significant determinants of brain damage:

A) Developmental stage of brain during insult,
B) Intensity of insult, and
C) Duration of the insult.

Figure 2:



Neurogenesis is the initial step in the development of the brain, which then progresses through a series of stages like neural migration, maturation, synaptogenesis, pruning, and myelin synthesis.

Anatomy of Visual Pathway (from Eyes to the Brain):

The transmission of the special sensory information necessary for vision is carried out by the optic nerve (CN II), the second cranial nerve.

It develops from the optic vesicle, an outpouching of the forebrain. Thus, one may regard the optic nerve as a component of the central nervous system.

The union of the optic nerves from each eye forms the optic chiasma, which is located in the middle cranial fossa. While fibers from the temporal halves of the retina stay ipsilateral, those from the nasal half of the retina cross over to the contralateral optic tract at the chiasma.

These optic tract fibres synapse at the Lateral Geniculate Body (LGB), a relay station situated in the thalamus, after each optic tract travels to its corresponding cerebral hemisphere.

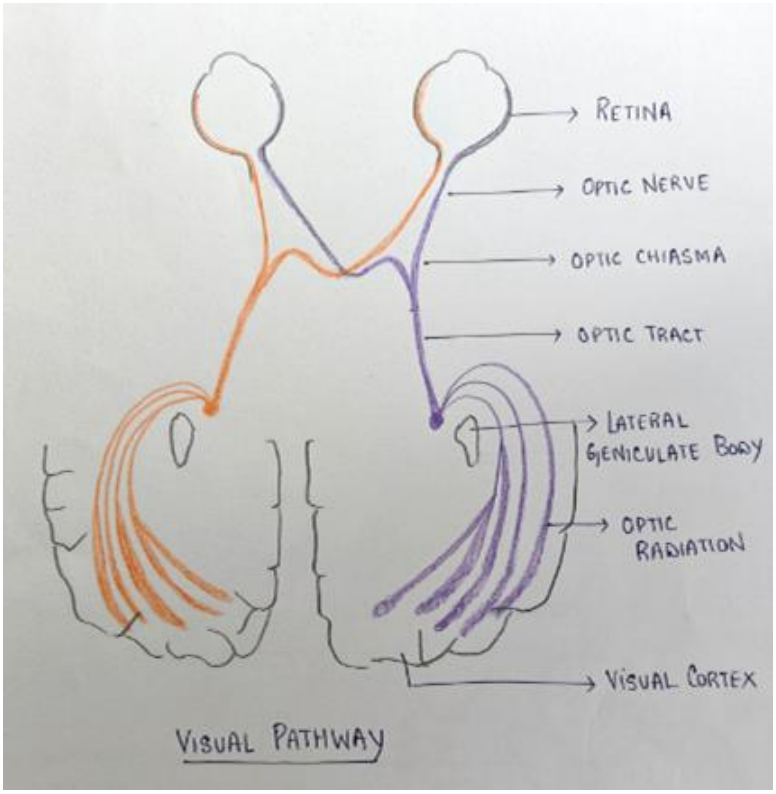
A collection of axons that convey visual information from the LGB make up optic radiation. .

The pathway itself can be divided into:

Upper optic radiation enters the visual cortex through the parietal lobe from the superior retinal quadrants, which correspond to the inferior visual field quadrants.

Lower optic radiation, which originates in the inferior retinal quadrants (which correspond to the superior visual field quadrants), passes through the temporal lobe and onto the visual cortex through a route called Meyer's loop.

Figure 3:



Disentangling the Brain Wiring: Visual cortex and Visual Association Areas

The awareness of visual stimuli is controlled by the primary visual cortex (V1), sometimes referred to as Brodmann's area 17. It is located in the occipital lobe, occupies the walls of the deep calcarine sulcus. The secondary visual areas 18 (V2) and 19(V3), which involve the occipital lobe and the posterior section of the parietal lobe, are located adjacent to the primary visual cortex. It is involved in the interpretation and identification of objects as well as the perception of motion, colour, depth, and other aspects of vision.

Table1

PRIMARY VISUAL PROCESSING AREAS OF BRAIN	FUNCTION
V1(plexiform lamina)	Transmitting information to the dorsal and ventral stream pathways
V2(external granular lamina)	Object recognition and attentional modulation
V3(pyramidal lamina)	Role in processing global motion
V4(internal granular lamina)	Colour information and form recognition
V5(ganglionic lamina)	Processing visual motion
V6(multiform lamina)	Spatially directed reaching movements

Ventral and dorsal stream

As visual information leaves the occipital lobe. It travels along two primary pathways, or "streams".

The ventral stream ("what pathway") leads to the temporal lobe, which is involved with object identification.
The dorsal stream ("how pathway") leads to the parietal lobe, which is involved with processing the object's spatial orientation.

While the dorsal stream, or "vision-for-action" circuit, has been predominantly linked to visually guided reaching. The ventral stream, or "vision-for-perception" pathway, is thought to primarily subserve the function of recognizing and discriminating of visual forms and objects.

According to a research by Dutton et al., CVI can result from either pathway malfunctioning, but dorsal stream dysfunction is more likely in CVI children.

Children with CVI frequently present with a wide range and combination of visual dysfunctions, such as reduced visual acuity and visual field abnormalities, depending on the variability in the location and extent of brain injury

Reduced visual acuity and visual perceptual dysfunction seen in congenital CVI have been linked to widespread and diffuse alterations in structural and functional integrity of gray and white matter pathways, including optic radiations from the optic nerves to the occipital cortex.[16]

Perinatal hypoxia-ischemic encephalopathy (HIE) is the most common cause of CVI in term babies. HIE sequelae are dependent on regional variations in vascular perfusion (like watershed zones). Deep grey matter, hippocampus, brainstem, thalamic regions are the areas most commonly affected in HIE. [13, 14]
The most common form of brain damage observed in preterm infants is periventricular leukomalacia, which is characterised by hemorrhagic necrosis in the periventricular white matter just dorsal and lateral to the external angle of lateral ventricle. [13, 15]
Lateral ventricles were linked with both cognitive, perceptual and motor issues, instead of being confined to visual perceptual problems and probably reflect the extensiveness of the brain damage. [17]

Study of neuroimaging in different phases of CVI would give a better picture of the pattern of involvement in different regions of the brain. This in turn suggests the association with perinatal insult. This could further lead to appropriate perinatal interventions to prevent future impairment.

Etiology of CVI

Pre natal

1) Maternal drug use
2) Intrauterine infections
3) Twin pregnancy
4) CNS developmental defect

Perinatal

1) Hypoxic- Ischemic Encephalopathy (HIE)
2) Periventricular Leukomalacia (PVL)
3) Cerebral hemorrhage

Postnatal

1) Head injury (Trauma)
2) Stroke
3) Seizures
4) Meningitis
5) Hydrocephalus

Maternal drug use

According to research by Mc Glone et al., 6-month-old babies exposed to methadone during pregnancy showed aberrant visual evoked potentials [18], which may indicate disturbance in the visual pathway. There have also been reports of abnormal visual cortical responses in a small subset of children exposed to amphetamines during pregnancy. [19]

Intrauterine infections

11.8% to 15% of cases of CVI are caused by infections that occur during the initial period of gestation that is upto 20 weeks. [20] The occipital cortex is more susceptible to damage produced by Haemophilus Influenzae, and hence, it is the most common organism causing CVI. Other causative agents include herpes simplex virus, meningococci, and pneumococci. Different mechanisms by which infection might injure the brain include thrombophlebitis, arterial occlusion, hypoxic-ischemic damage, venous sinus thrombosis and hydrocephalus.

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Perinatal hypoxic ischemia

It is the most common cause of CVI, accounting for a significant majority of cases. [14, 20, 21]

The type and extent of brain injury resulting from this condition largely depend on the timing of the insult, and it differs between term and preterm infants.

In term infants, watershed zones of the cerebral cortex are affected. The hypoxia leads to reduced blood flow in these areas, causing infarction in the frontal and parieto-occipital regions (parasagittal regions). The striate cortex responsible for visual processing is also frequently involved.

In the case of a preterm of 24-34 weeks gestation, germinal centers in periventricular white matter are affected. The germinal centers generate glial cells and neuronal cells that migrate towards the cerebrum.

Hypoxic brain injury is explained as follows, hypoxia causes ischemia, which causes focal tissue damage in immature watershed zones especially the periventricular white matter region leading to PVL. Ischemia can occur due to locally decreased blood flow in the brain which happens in the case of cerebral hemorrhage, premature newborns are at risk for this type of injury. [22]

Perinatal strokes and postnatal hypoxia commonly lead to hemiplegic cerebral palsy. Concurrent hypoxic incidents can cause CVI, as a consequence of reduced blood supply to the retrochiasmal pathway. [23]

Hydrocephalus can originate in all time periods and causes both anterior and posterior visual pathway damage.

CVI can be associated with *congenital brain malformations* like lissencephaly, holoprosencephaly, schizencephaly, polymicrogyria, pachygyria and porencephaly. [24]

Metabolic disorders: It is observed in conditions such as maple syrup urine disease as well as in conjunction with neurodegenerative diseases like Tay-Sachs, Leigh's disease, neuronal ceroid lipofuscinosis and X-linked adreno leukodystrophy

Epilepsy: CVI can manifest as a result of postictal hypoxia or increased metabolic demands. CVI in children with multiple disabilities often present with epileptiform discharges affecting the occipital lobes.

CVI and MRI (Imaging of the brain):

Magnetic resonance imaging (MRI), a non-invasive imaging modality, is a highly effective diagnostic tool for the brain abnormalities because of it's remarkable soft-tissue resolution. It uses a strong magnetic field and radio waves to create detailed images to produce high quality two-dimensional or three-dimensional images of the brain and brainstem as well as the cerebellum and exhibits remarkable diagnostic accuracy. MRI was performed with a super conductive system operating at 3 Tesla. 5mm thick images with a 1mm interslice gap in the axial, coronal and sagittal planes were considered. Because of the radiation burden from CT-scans in children and the fact that ultrasound is not possible after the age of 1 year, MRI is the investigation of choice for these children.

The distinct patterns of brain structure involvement in various disorders is attributed to selective susceptibility of brain structures. MRI is superior in detecting subtle changes. According to a study done by Boonstra FN et al, in children with CVI, imaging is part of the diagnostic possibilities. An inventory of the damage to the brain regions involved in visual processing could be made using MRI. [25]

Hoyt and Taylor stated that CVI can manifest as a number of different brain abnormalities such as embryological abnormalities (Encephalocele, holoprosencephalies), cortical developmental anomalies, periventricular leukomalacia (PVL), periventricular and intraventricular hemorrhages, neonatal encephalopathy, or cerebral ischemia during the perinatal period as well.The visual pathways may be harmed by certain brain abnormalities that occur at birth.[25,26]

In a systemic review done by Philip SS et all periventricular leucomalacia on MRI was found to have a strong association with CVI in all 30 studies.[27] White matter damage due to oxygen deprivation is seen in preterm children, while gray matter damage (cortex) is seen in full-term children. Perinatal hypoxia-ischemic encephalopathy (HIE) is the most common cause of CVI in term infants. HIE sequelae are dependent on variations in vascular perfusion across different regions (such as watershed zones). The brainstem, thalamus, hippocampal, and deep grey matter are the areas most commonly damaged in HIE. [13, 14]

The most common type of brain damage in premature infants is periventricular leukomalacia, which is associated with hemorrhagic necrosis in the periventricular white matter just dorsal and lateral to the external angle of lateral ventricle. [13, 15]

Studies using magnetic resonance imaging (MRI) can predict various patterns of the subsequent neurodevelopmental outcomes.[28, 29] Acute and severe insults are often linked to gray matter damage in the central nervous system, which severely impairs motor and cognitive function. Lesions in the vascular watershed zones in cases of subacute or chronic hypoxia-ischemia are often linked to intermediate outcomes. [28, 30-34]

In children with CVI, the usefulness of neuroradiological imaging is still unclear. Guidance is warranted for the application of neuroradiological examination in this population and its role in the diagnosis CVI.
Several authors (Whiting et al, Lambert et al, Flodmark et al) have investigated the possibility of predicting the severity and duration of CVI by brain imaging in children with inconsistent results.[2,35]

Due to the lack of consistent correlation between visual impairment and structural changes observed in neuroimaging in children with CVI, researchers have sought to employ functional neuroimaging techniques such as functional MRI (fMRI), positron emission tomography (PET), and single-photon emission computerized tomography (SPECT) in an effort to image these patients.

MATERIALS AND METHODS:

Materials and Methods:

Study Center: KLES Dr. Prabhakar Kore Hospital and Medical Research Center in Belagavi has a specialized CVI Clinic in the ophthalmology department.

Study Design: Prospective Study, Cross-sectional, Hospital based study.

Study Duration: 1st August 2022 to 31st July 2023

Subjects: Subjects attending KLEs Dr Prabhakar Kore hospital, Belagavi from August 2022 to July 2023. Subjects aged one to four years attending the Child Development Clinic in the Pediatric department and diagnosed with Cerebral Visual Impairment without ocular pathologies or ocular pathologies not attributing/ explaining the visual impairment were evaluated and enrolled for the study.

Sample size:

Below formula was used for sample size calculation:

$$n = \left[\frac{\left(Z_{1-\alpha/2} + Z_{1-\beta}\right)}{C}\right]^2 + 3$$

Where ***C*** was calculated as,

$$C = 0.5 \times log_e\left({(1+r)}/{(1-r)}\right)$$

Where *n* was the sample size required, $Z_{1-\alpha/2}$ was the normal distribution value corresponding to level of significance, $Z_{1-\beta}$ is the normal distribution value corresponding to the power. *r* is the correlation coefficient.

We assumed the correlation between visual acuity and total brain score as 0.5 and with 95% confidence level and with 80% power minimum sample size required was:

$$C = 0.5 \times log_e \left({(1 + 0.5)} \Big/ {(1 - 0.5)} \right)$$

$$C = 0.5493061$$

$$n = \left[\frac{(1.96 + 0.84)}{0.5493061} \right]^2 + 3$$

$$n = 26.0123 + 3$$

$$n = 29.0123$$

Minimum sample size required was 29.

Sampling Technique: Non Probability Purposive Sampling

Inclusion Criteria:

1. Children from one to four years of age
2. Diagnosis of Cerebral visual impairment

Exclusion Criteria:

Children aged one to four years with cerebral visual impairment due to ocular pathologies such as corneal opacity, strabismus, amblyopia owing to glaucoma, old optic neuritis, retinal dystrophies, and degeneration, congenital globe anomalies (microphthalmos/anophthalmos) etc is for exclusion.

Data Collection:

A cross-sectional study of 35 children between one to four years of age attending the child development clinic diagnosed with CVI and referred to Ophthalmology OPD of KLE's Dr Prabhakar Hospital was conducted. Ethical clearance was obtained from Institutional Ethics Committee prior to the commencement of the study. Informed Formal written consent in English /Kannada /Marathi was taken from all parents of children enrolled in the study.

A detailed history including ocular complaints, characteristic visual behaviour, antenatal history, mode of delivery, gestational age, birth weight, perinatal and postnatal history, milestones, and consanguinity among parents was taken.

Visual acuity was recorded with the forced choice preferential looking test i.e by means of Teller's Acuity Card test.

Teller's acuity cards, a type of forced- choice preferential looking test were used for the quantitative assessment of vision in our study

The visual acuity tested with Teller's acuity cards was then categorized, depending on cycles per cm as very low, low and near normal vision. [21]

Very low vision - < 1.6 cy/cm
Low vision – 1.6cy/cm – 9.6 cy/cm
Near normal – 9.6 -26.0 cy/cm

Visual Acuity Assessment

Normal visual acuity in various age groups are-

- At birth - 6/120 (20/400)
- Four months-6/60 (20/200)
- Six months-6/36 (20/120)
- One year-6/18 (20/60)
- Two years- 6/6 (20/20)

When evaluating a child's visual acuity, it takes longer than normal and demands patience.

Visual acuity assessment methods

Fixation

Normally the fixation should be central, steady and maintained (CSM)

PHOTOGRAGH:1

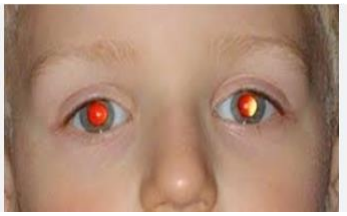
Menace Reflex

Menace reflex is the reflex blinking that happens when something moves quickly or when there is visual threat. By five months of age, the reflex develops.

Bruckner's reflex

Bruckner's reflex can be useful in quickly identifying refractive errors. It is a rapid screening method.

PHOTOGRAPH:2



Preferential Looking Test

When offered an option between a plain and patterned surface, the infant prefers towards the patterned surface.

Teller's acuity cards

The screen is made up of one side with a uniform surface and the other side with randomly placed black and white stripes. The infant faces the screen, and as it responds to the patterned stimuli, the observer notes the direction of the baby's head and eye movements.

PHOTOGRAPH:3

Lea's gratings

Lea gratings are preferential looking test used to evaluate visual acuity of infants and children with disability.

Anterior Segment Examination

The Hirschberg's test was used to evaluate the visual axes. The cover–uncover test was performed to rule out strabismus. Uniocular and binocular movements were examined. The presence or absence of nystagmus was noted. All subjects underwent a thorough ocular examination including anterior segment examination and dilated fundoscopy to rule out any ocular pathologies.

Detailed CVI evaluation was done following ten visual behavioural responses, these were assessed routinely, based on the assessment method drawn from profoma by **Christine Roman- Lantzy**. [36]

CVI Evaluation:

- Color preference
- Need for movement
- Visual latency
- Visual field preferences

- Light-gazing and non-purposeful gaze
- Decreased distance viewing
- Atypical visual reflexes
- Novelty
- Complexity
- Visual-motor

Based on CVI characteristics, the most widely used scale to evaluate visual functioning in children with CVI is the CVI Range, developed by Roman-Lantzy.

The scoring of the CVI Range involves two main components. The **Across-CVI Characteristics method**, which is the first section, provides valuable insights into the child's visual abilities across various visual functional levels.

"Five levels of visual functioning are :

CVI Range 1-2: Minimal visual response;

CVI Range 3-4: More consistent visual response;

CVI Range 5-6: Using vision for functional tasks;

CVI Range 7-8: Demonstrates visual curiosity; and,

CVI Range 9-10: Spontaneously uses vision for most functional activities."[41]

The **Within-CVI characteristics approach** is the second section of the CVI Range assessment. Each trait is given an individual score in this section to determine the degree to which it impacts the child's visual functioning. A scoring scale from zero to one is used for each characteristic.

"0 = not resolved/ constant influence on visual functioning;

0.25 = resolving;

0.5 = resolving; occasionally affecting visual functioning;

0.75 = resolving; and,

1 = resolved; that a factor is not influencing visual functioning."[41]

Finally, the overall range of visual functioning is determined by comparing, the scores obtained from the Across-CVI characteristics Method and the Within-CVI Characteristics Method and a score ranging from one to ten is given. To determine the degree of severity, CVI children are divided into three phases based on this score. Different intervention strategies are recommended depending on the specific CVI phase.[36]

Table2:

CVI Phase	Score
Phase I	0 – 3.5
Phase II	3.5 – 7.5
Phase III	7.5 – 10

MRI SCORING

A reliable and validated semi quantitative scale designed by Fiori et al for assessing brain lesion severity in children was used to categorize the results of MRI scans. [6]

Using this pre-designed scoring, MRI scoring was done, made adaptive to our local standards and validated.

Using the semi-quantitative coding template for MRI brain scan, this study intends to consider the relationship between brain lesions in different regions of the brain and relationship with visual acuity and phase of CVI. [6, 7]

Children with CVI undergo MRI brain screening according to standard protocol which was evaluated using a standard radiological template. Results were then coded according to a modified version of the validated semi quantitative template from a previous study (Fiori et al.)

These summary scores can be summed for a total score.

CEREBRAL LOBE

Each lobe - frontal, parietal, occipital, temporal, and striate - were scored separately. Cortical gray matter and subcortical white matter for each lobe were assessed (0 being no anomaly, 1 being an abnormality found), and the scores were added up to get a lobar score (0–2) for each hemisphere.

BRAINSTEM

The brainstem was coded as 1=observed abnormality and 0= no abnormality

CEREBELLUM

A score of 0–3 was obtained by adding the codes for left hemisphere, right hemisphere and vermis of the cerebellum (0 = no abnormality, 1 = abnormality found.

VISUAL PATHWAY

The visual pathways were coded separately in this study because of interest in vision. Three regions were considered: the pregeniculate area (optic nerves, optic tracts), postgeniculate area (optic radiations) and visual cortex. Each region was coded (0= no abnormality, 1= abnormality seen) and summed for a visual pathway score ranging between 0 and 3.

MRI score out of a total of 27 was calculated

Data will be collected and stored in Microsoft Excel. Data will be analyzed using statistical software R and Microsoft Excel. Continuous variables will be given in mean ± SD/median (range). Categorical variables will be represented by frequency.

METHODS:

Data is analyzed using statistical software R version 4.3.2 and Microsoft Excel. Categorical variables given in the form of frequency tables. Continuous variables given in Mean ± SD / Median (Min, Max) form. Normality of variable is checked by Shapiro Wilk test and Q plot. When the data follows normal distribution, parametric tests are used. Otherwise, non-parametric test is used. Two sample t test is used to compare mean of MRI score over different variables. One-way ANOVA is used to compare mean of MRI score over CVI phases. Kruskal Wallis test is used to compare the distribution of MRI score over refractive error. Pearsons's correlation test is used to check the correlation of birthweight with MRI score. Spearman's rank correlation test is used to check the correlation of age and vision with MRI score. P-value less than or equal to 0.05 indicates statistical significance.

RESULTS:

This study was conducted in a tertiary care teaching hospital of North Karnataka from August 2022 to July 2023.

Analysis was done for data of 35 CVI children whose age ranged from one to four years with mean age of 2.33 ± 1.29 years. Evaluation was done for all variables and results are presented as below.

Table 3: Demographic details.

Variables	Sub Category	Number of children
Age (years)	≤ 3 years	25
	> 3 years	10
Sex	Female	8
	Male	27

Table 3: Reveals the demographics that 25(71.42%) of the children were below the age of 3 years and 27(77%) were male

Table 4: Birth history.

Variables	Sub Category	Number of children (%)
Gestation Age	Preterm	7 (20%)
	Term	28 (80%)
Birth Weight (Kg)	<1.5kg	1 (2.86%)
	1.5-2.5kg	17 (48.57%)
	>2.5kg	17 (48.57%)
Type of Delivery	LSCS	16 (45.71%)
	Normal	19 (54.29%)

Table 4: Reveals the birth history that 28 (80%) of the children were term and most of them had birth weight more than 1.5 kg.

Table 5: Post Natal history

Variables	Sub Category	Number of children (%)
NICU Admission	Absent	9 (25.71%)
	Present	26 (74.29%)
Oxygen Therapy	No	16 (45.71%)
	Yes	19 (54.29%)
Jaundice	No	20 (57.14%)
	Yes	15 (42.86%)
Convulsions	No	16 (45.71%)
	Yes	19 (54.29%)
Hypoglycemia	No	26 (74.29%)
	Yes	9 (25.71%)

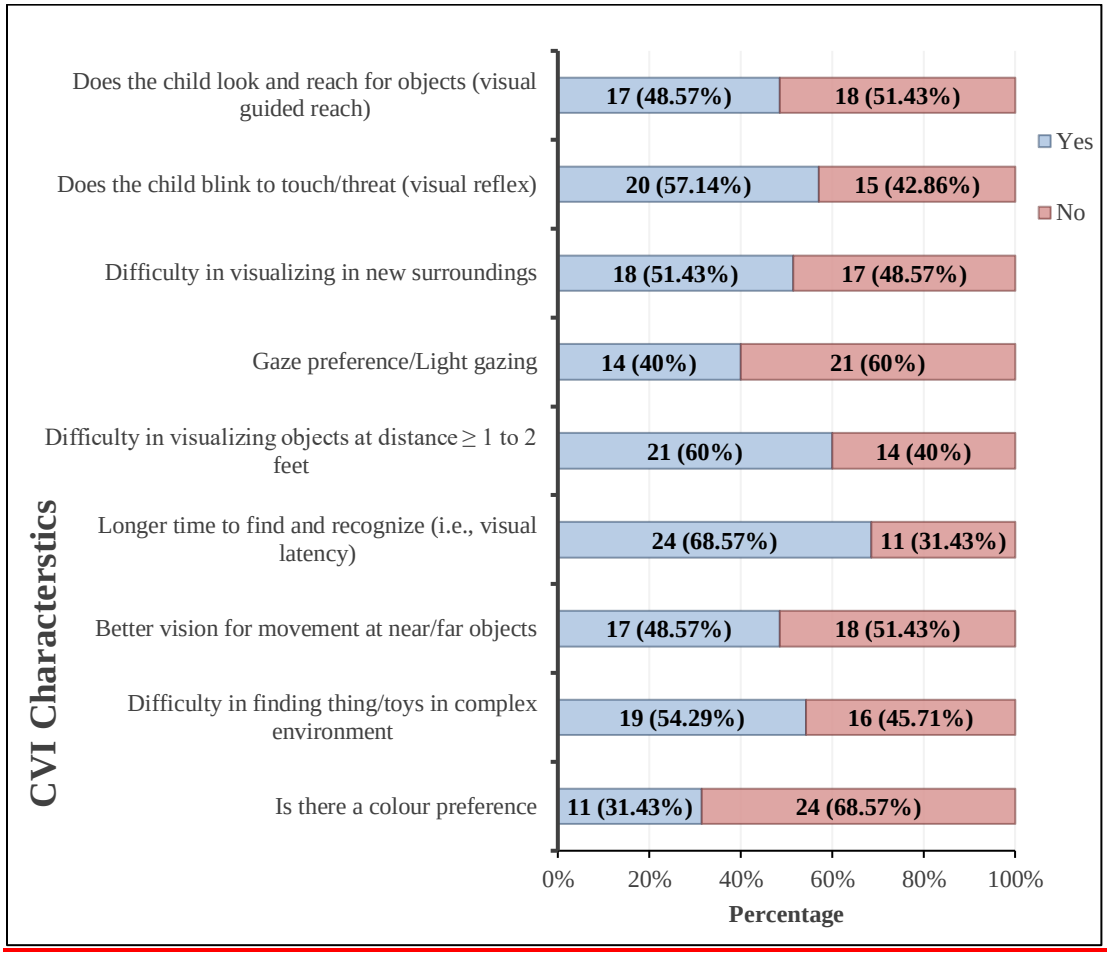
Table 5: Reveals the post natal history that out of 35 children, **26 (74.29%) children had history of NICU admission**.

There was no history of chorioamionitis in any child.

It was also observed that Development Milestones were delayed in 34 (97.14%) children.

Among 35 children, consanguineous marriage history was present in parents of 10 (28.57%) children

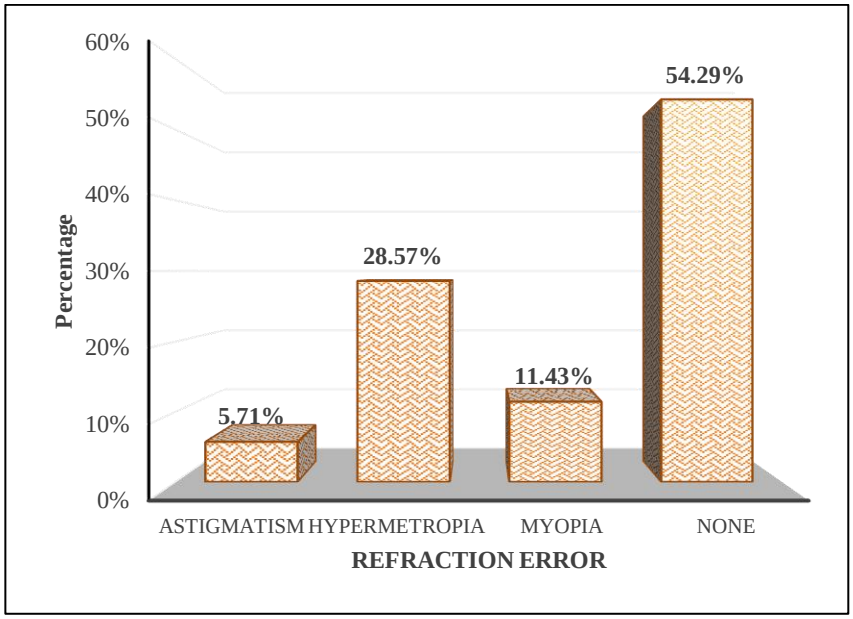
Graph 1: CVI Characterstics



Graph 1:

It reveals that 19(54.29%) children face difficulty in finding things or toys in complex environment.
Also a significant number of children 24(68.57%), experience latency.
Difficulty in visualizing objects at a distance of more than two feet is reported by 21 (60%) children.

Graph 2: Distribution of children according to refraction error.



Graph 2: Reveals that 19(54.29%) children in the study were emmetropic. While the most common refractive error seen in the children was hypermetropia in 10 children.

Further on ***anterior segment examination*** of the CVI children in our study it was observed that 22 (62.86%) children had orthophoria while 13 (37.14%) children had strabismus out of which 9 children had exotropia.

Also nystagmus was seen in only 9 (25.71%) children

Table 6: Fundus Findings.

Variables	Sub Category	Number of children (%)
Post Segment	Temporal pallor	6 (17.14%)
	Pale disc	5 (14.28%)
	Small hyperopic disc	4 (11.42%)
	Optic nerve hypoplasia	3 (8.57%)
	Within normal limits	17 (48.57%)

Table 6: Reveals the most common significant posterior segment finding noticed was temporal pallor of disc in 6 children closely followed by pale disc observed in 5 children.

Table 7: Distribution of children according to pediatric diagnosis.

Pediatric diagnosis	Number of children (%)
Cerebral palsy	15(42.86%)
Global developmental delay	15 (42.86%)
Epilepsy	4 (11.42%)
Neurodegenerative disorder	1 (2.86%)

Table 7: Shows that most of the children in the study were either having cerebral palsy or global developmental delay.

Table 8: Distribution of children according to CVI phase.

CVI Phase	Number of children (%)
I	17 (48.57%)
II	10 (28.57%)
III	8 (22.86%)

Table 8: Shows that most of the children in the study were in CVI phase I on evaluation

Table 9: Distribution of children according to MRI findings.

Variables	Sub Category	Number of subjects (%)
Right hemisphere *(lobes involved)	Frontal	10 (2.86%)
	Parietal	24 (11.43%)
	Occipital	18 (5.71%)
	Temporal	8 (2.86%)
	Striatum	2 (5.71%)
Left hemisphere *(lobes involved)	Frontal	10 (2.86%)
	Parietal	25 (11.43%)
	Occipital	18 (2.86%)
	Temporal	9 (2.86%)
	Striatum	2 (2.86%)
Cerebellum	Involvement	4 (5.71%)
Visual pathway	Involvement	15 (42.86%)
Right hemisphere (MRI score)	Any lobe involvement	29
Left hemisphere (MRI score)	Any lobe involvement	31

** There could be more than one lobe involvement in some children which is documented and scored considering all lobes which were involved*

Table 9: According to this most commonly parietal lobe involvement on MRI is seen followed by occipital, frontal and temporal lobe respectively. Visual pathway involvement on MRI was observed in 15 children.

-Cerebellum involvement in the form of vermis and hemisphere was seen in 4 children which was symmetrically affected.

-Further it is observed that both cerebral hemispheres are symmetrically involved in most of the children, except in 2 children where left hemisphere involvement is more as compared to right hemisphere

Table 10: Comparison of MRI score over perinatal history

Variables	Sub Category	MRI Score		p-value
		Mean ± SD	Median (Min, Max)	
Gestation Age	Preterm	3.86 ± 2.48	3 (1, 7)	0.3213[t]
	Term	4.89 ± 2.42	5 (0, 9)	
Type of Delivery	LSCS	4.94 ± 2.72	4.5 (0, 9)	0.5822[t]
	Normal	4.47 ± 2.22	5 (0, 8)	
NICU Admission	Absent	4.78 ± 2.54	5 (0, 8)	0.8976[t]
	Present	4.65 ± 2.45	4.5 (0, 9)	
Oxygen Therapy	No	5.12 ± 2.25	5 (0, 8)	0.3347[t]
	Yes	4.32 ± 2.58	4 (0, 9)	
Jaundice	No	5.25 ± 2.59	5 (0, 9)	0.1146[t]
	Yes	3.93 ± 2.05	4 (0, 7)	
Convulsions	No	4.69 ± 2.85	5 (0, 9)	0.9969[t]
	Yes	4.68 ± 2.11	4 (1, 8)	
Hypoglycemia	No	4.5 ± 2.69	4 (0, 9)	0.4513[t]
	Yes	5.22 ± 1.48	5 (3, 8)	

Abbreviation: t- Chi-Square test.

Table 10: It is observed that there is no significant difference in mean MRI score over Gestation Age, Type of Delivery, NICU Admission, Oxygen Therapy, Jaundice, Convulsions, and Hypoglycemia.

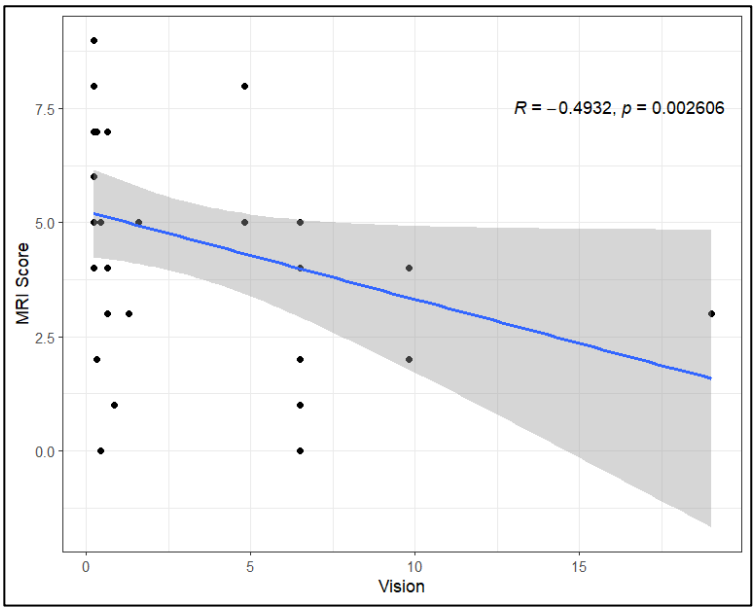
Table 11: Correlation of age, birth weight, vision with MRI score.

Variables	Correlation coefficient	p-value
Age (years)	-0.1926	0.2676^{SP}
Birthweight (Kg)	-0.0679	0.6985^{SP}
Vision	-0.4932	$\mathbf{0.0026^{SP}*}$

*Abbreviation: SP – Spearman's rank correlation test, * indicates statistical significance.*

Table 11: It is observed that, **there is significant moderate negative correlation between vision and MRI score** (p-value = 0.0026). However, there is no significant correlation between age and birthweight with MRI score

Graph 3: Variation of vision with MRI score.



Graph 3: It shows a negative correlation between MRI Score and Vision.

So it can be concluded that children with very low vision had a higher MRI Score.

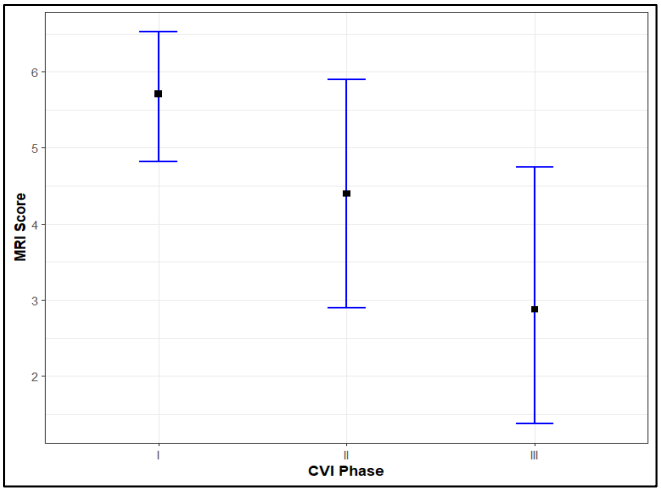
Table 12: Comparison of MRI score over CVI Phase

Variables	Sub Category	MRI Score		p-value
		Mean ± SD	Median (Min, Max)	
CVI Phase	I	5.71 ± 1.86	5 (2, 9)	**0.018[A]***
	II	4.4 ± 2.5	4 (0, 8)	
	III	2.88 ± 2.53	2.5 (0, 8)	

*Abbreviation: A – One-way analysis of variance(ANOVA), * indicates statistical significance*

Table 12: It is observed that, there is significant difference in mean MRI score over CVI phase

Graph 4: Mean plot of MRI score over CVI phase.



Graph 4: Further, from Tukey's HSD(honestly significant difference), it is observed that the **MRI score in those children in CVI phase I is significantly larger than the MRI score of those children in CVI phase III** (p-value = 0.0146).

Table 13: Comparison of Temporal Lobe, Parietal Lobe and Occipital Lobe Involvement over CVI phases.

Variables	CVI phases			p-value
	I	II	III	
Temporal Lobe	4 (23.53%)	4 (40%)	1 (12.5%)	0.4303^{MC}
Parietal Lobe	14 (82.35%)	7 (70%)	4 (50%)	0.2844^{MC}
Occipital Lobe	12 (70.59%)	6 (60%)	1 (12.5%)	$\mathbf{0.02899^{MC}*}$

*Abbreviation: MC – Chi square test with Monte Carlo simulation, * indicates statistical significance.*

Table 13: It is observed that, there **is significant association of occipital lobe involvement with CVI phases.** There is no significant association of temporal and parietal lobe with CVI phases.

DISCUSSION:

The present study, " Correlation of different phases of CVI in children aged one to four years with MRI" was conducted in a tertiary care teaching hospital in Karnataka from August 2022 to July 2023. To our knowledge this is the first study that correlates brain lesions severity and phase wise severity in CVI. It was a cross-sectional study comprising a total of 35 children diagnosed with CVI. Their visual acuity was evaluated with preferential looking test (TAC). Detailed CVI evaluation was done following ten visual behavioural responses and characteristics. This assessment method was drawn from the proforma of Christine Roman- Lantzy. CVI Phases were calculated and correlated with MRI scoring.

Present study consisted of 27 (77.14%) boys and 8 (22.86%) girls having CVI. This large difference in male to female could be attributed to the more care given to male children in the society. Majority in our study were in the age group less than or equal to three years (71.42%)

In our study majority were term babies (80%). Birth weight of 97.14% of the children was more than 1.5 kg. There was no a direct correlation between phases of CVI and gestational age. These findings suggest that the severity of phases does not differ significantly between term and pre-terms and it was independent of the birth weight. However growing evidence points to cerebral visual impairment (CVI) emerging as the most common cause of vision impairment in childhood. Children born prematurely have a serious risk of brain injury, which can result in conditions like cerebral palsy and low IQ.

Post natal history showed that out of 35 children 26 (74.29%) children had history of NICU admission and developmental milestones were delayed in 34 (97.14%) children.
Among 35 children, consanguineous marriage history was present in parents of 10(28.57%) children. CVI phases were independent of consanguinity in our study.

Response of parents regarding symptoms of functional vision difficulties suggestive of CVI characteristics observed in daily life among their children was recorded. 68.57% told that their child had visual latency that is they took longer time to find and recognise objects, 60% children had difficulty in visualizing objects at a distance of more than two feet inspite of good visual acuity.54.29% children had difficulty in finding toys in a complex environment.

In the context of CVI, refractive error may coexist and it is important that child undergoes a comprehensive ocular examination for any potential refractive errors. In our study 54.28% were emmetropic and 45.72% had refractive error. Majorities (28.57%) were hyperopes, followed by myopia (11.43%) and mixed astigmatism (5.71%). Similar results were obtained in an Indian study done by

Pehere NK in 142 children, 50% had significant refractive error; among which 50 % had myopia 46% had hyperopia, and 2.8% had mixed astigmatism.[37] In a study by Fazzi et al majority were hyperopes (29 %), followed by astigmatism (21%) and myopia (11%).[7]. Appropriate spectacle correction was given to all the children with refractive error. It is important to understand that correcting refractive errors with spectacles alone will not solve all the visual challenges associated with CVI, other interventions such as visual stimulation and rehabilitation to optimize visual functioning are essential.

In our study 13(37.14%) children had strabismus out of which 9 children had exotropia. Nystagmus was seen in only 9 children in our study. In a study done by Huo et al in 170 CVI children, 37% had squint.[20] Huo et al also mentioned that 11.1% out of 170 CVI children had nystagmus and Fazzi et al found that 35.5% in their respective studies.[20, 21] Nystagmus was seen in only 9 children in our study.

In our study out of 35 children, 18 had optic disc changes with majority showing optic disc pallor followed by pale disc, small hyperopic disc and optic nerve hypoplasia. Huo et al and Ruberto et al have mentioned optic atrophy and optic nerve hypoplasia as optic disc findings in CVI in their respective studies. [20, 38]

The results are similar to study done by Fazzi et al on children with CVI, the optic disc findings revealed that out of 121 patients, 53 had optic disc changes, with majority showing temporal optic disc pallor followed by optic atrophy, large optic disc cups and optic nerve hypoplasia.[21] This warrants further studies on the correlation of optic nerve pallor with MRI Score

Most common paediatric diagnosis seen in these children with CVI was Cerebral Palsy and Global Developmental Delay (GDD) emphasizing that CVI is a result of failure of development of various domains such as motor, cognitive, speech and others. In cerebral palsy, areas in brain which are injured and lead to motor deficits are anatomically closely related to the visual perception brain area. Thus it is not surprising that the incidence of CVI within the CP population is so high. About two-thirds of children with cerebral palsy were found to be associated with CVI in an African study, showing 47.7% prevalence and an Indian study showing 28% association.[39]

The high incidence of CP and GDD in our study showed no relation with the severity of CVI

A review by Ospinia suggest that hypoxia in term infants tends to cause frontal and parieto-occipital infarctions.[22] .According to our study on MRI Scoring, it was observed that parietal lobe was most common involved followed by occipital, frontal and temporal lobe respectively. Parietal lobe involvement on MRI was more common as compared to temporal lobe signifying the dorsal pathway involvement. Dysfunction of either of the pathways can lead to CVI, while dorsal stream dysfunction is more common in CVI children according to study done by Dutton et al. [40] The results are consistent with earlier research,

which indicates that children with CVI have widespread brain involvement, with the majority involving the occipital and parietal areas.[16, 17,41-43] Similar findings were seen in a research by Sakki et al., wherein half of the children (43–54%) showed abnormalities in frontal or temporal hemispheres, or striatum The occipital or parietal regions of about 71%–79% that is approximately three quarters of participants had abnormalities Cerebellar abnormality was reported in five participants (18%) and brainstem abnormality in four participants (14%) showing a similar trend of brain involvement but in contrast to our study this study did not reach statistical significance. [7]Further it was observed that both cerebral hemispheres were symmetrically involved in most of the children, except 2 children where left hemisphere involvement was more as compared to right hemisphere.

It was observed in our study that MRI Scores were not related to gestational age and NICU admission. According to a study done by Tinelli F et al while comparing location of cortical damage, a positive correlation was seen between occipital lobe damage and total visual score, while no significant correlation was found with frontal, temporal and parietal lobes involvement.[43] In our study significant negative association was noted between visual acuity and MRI Score. It was observed in our study that children with very low vision had a higher MRI Score. The outcomes are comparable to those of Tinelli et. (2020), who had employed a similar MRI coding template to ours and found a strong correlation between visual functional impairment scores and global brain lesion severity on MRI scans in children with cerebral palsy and periventricular leukomalacia.[43] In contrast to Tinelli et al., who employed single encompassing categoryof visual dysfunction that included fixation, nystagmus, visual acuity, fields and stereopsis, our study concentrated purely on preferential looking test(TAC), which is highly quantitative.

Association of brain lesions with CVI is well established but it was observed that the MRI score in those with CVI phase I was significantly larger than the MRI Score of those with CVI phase III(p-value = 0.0146). High score means multiple lobe involvement including damage to visual association areas. This could be the explanation for the inverse relationship between CVI Phase and MRI Score.

Studies comparing different lobe involvement with severity of CVI are sparse. Though there is an increasing trend of parietal lobe and thereby dorsal pathway involvement in all the phases of CVI, significant association was found only between occipital lobe and CVI phases. This corresponds to Tinelli study too found a true correlation of occipital lobe with visual score. This suggests a theory that though visual association areas and dorsal and ventral pathways are the major culprits of functional visual impairment, a good functioning occipital lobe plays a crucial role in CVI and it’s severity. Functional MRI comparing visual association area scores would lead to further categorization of CVI and plan timely action for these children.

STRENGTHS OF OUR STUDY

-MRI was done for all the study participants.
-MRI was reviewed by both neuropaediatrian and radiologist, detailed scoring revealed significant co-existing neurological conditions in many patients.

LIMITATIONS

Since this was hospital based study, convenience sampling was done and only children diagnosed with CVI visiting the hospital are taken into consideration. Hence, there is a good internal validity of the study but study results cannot be generalized.
In view of growing brain, sample was restricted to age constraint of one to four years. As majority of the children were below the age of three, the findings of the study cannot be generalised to all age groups warranting further age wise comparison of MRI findings in CVI children.

CONCLUSION

- It is observed that the MRI score in those with CVI phase I is significantly larger than the MRI score of those with CVI phase III (p-value = 0.0146).
- There is significant moderate negative correlation between vision and MRI score (p-value = 0.0026).
- There is significant association of occipital lobe with CVI phases.(when compared between parietal, temporal and occipital lobe)

In conclusion, this study contributes to our understanding of the correlation between MRI Score and CVI Phase in children. It emphasises that CVI is a complex condition involving multiple factors and domains of visual function. Further research and comprehensive assessments are necessary to fully comprehend the visual impairments in CVI. A study involving children of various age groups done at multiple - centers involving diverse populations could provide a more robust understanding of the relationship between MRI Scoring with CVI phase.

SUMMARY

The present study aimed to evaluate the correlation of different phases of Cerebral Visual Impairment with MRI. The study was conducted at a tertiary care centre in South India and included 35 children who were diagnosed with CVI. Majority of children in the study were boys and most of the children were in age group of 1 to 3 years.

Factors such as prematurity, postnatal history, including oxygen therapy, neonatal jaundice, and hypoglycemia, did not show a significant association with MRI Score.

MRI Scoring did not significantly vary with age, indicating that brain development and maturation can differ during different stages of life and different phases of CVI.

The study findings revealed that on posterior segment evaluation there were Optic disc changes such as temporal pallor, pale optic disc, optic nerve hypoplasia and Small hyperopic disc .

The study also highlighted that delays in multiple areas of development, such as motor, cognitive, speech and others, are commonly observed in children with CVI. Global developmental delay and Cerebral palsy was found to be associated with CVI in a significant proportion of cases.

In the study it is observed that most commonly parietal lobe was involved followed by occipital, frontal and temporal lobe respectively and there is significant association of occipital lobe involvement with CVI Phases.

While MRI score is related to vision, so we can conclude that functional vision can be affected if there are underlying structural changes or damage to the visual pathways or processing centres. Visual acuity is a very important aspect of visual function, which inversely correlates with the MRI score. The presence of other conditions such as refractive errors, squint or nystagmus, together named Ocular Visual Impairment (OVI) can co-exist with CVI and contribute to visual impairment. A deeper understanding of various lobes involvement secondary to perinatal injury and the human visual system may allow us to interfere early, potentially leading for greater recovery.

Vision evaluation in CVI children involves assessment of various components like visual fields, visual attention span, visual motor integration and much more than just visual acuity.

The MRI score in those with CVI Phase I is significantly larger than the MRI score of those with CVI phase III
In summary, this study contributes to our understanding of the correlation

between MRI Score and CVI Phase in children. It emphasizes that CVI is a complex condition involving multiple factors and domains of visual function.

Further research and comprehensive assessments are necessary to fully comprehend the visual impairments in CVI. A study involving various age group of children done at multiple - centres involving diverse populations could provide a more robust understanding of the relationship between MRI Scoring with CVI phase.

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ANNEXURES I – ETHICAL CLEARANCE

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed to be University)
Accredited 'A+' Grade by NAAC in (3rd Cycle) Placed in Category 'A' by MHRD (GoI)
JNMC INSTITUTIONAL ETHICS COMMITTEE
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
Website: http://www.jnmc.edu
E-Mail : deme@jnmc.edu
Phone: (+ 91-(0)831 Office : 2472550
Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref No.MDC/JNMCIEC/87 **Date: 27/09/2022**

To,

BK0121003
PG Student in Ophthalmology,
J. N. Medical College,
BELAGAVI.

Sub: Institutional Ethical Clearance for the study.

With reference to the above, we wish to inform you that your proposed research project titled **"CORRELATION OF DIFFERENT PHASES OF CVI IN CHILDREN AGED 1 TO 4 YEARS WITH MRI: A ONE YEAR CROSS SECTIONAL STUDY."** is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee.

(Dr. Smita Sonoli)
Member Secretary
JNMC Institutional Ethics Committee
J.N.Medical College, Belagavi.

(Dr. Harsha Hegde)
Chairman,
JNMC Institutional Ethics Committee
J.N.Medical College, Belagavi

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ANNEXURE II – CONSENT FORM

INFORMED CONSENT

KAHERs JNMC
BELAGAVI

TitleofResearch:

"TITLE OF THE PROJECT/STUDY"

"CORRELATION OF DIFFERENT PHASES OF CVI IN CHILDREN AGED 1 TO 4 YEARS WITH MRI : A ONE YEAR CROSS SECTIONAL STUDY AT KLES DR. PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE "

Name of Student/Principal Investigator :

POST GRADUATE STUDENT
(M.S OPHTHALMOLOGY)
JNMC, BELAGAVI.

Name of Guide/Co Investigators:

PROFESSOR
DEPT. OF OPHTHALMOLOGY,
JNMC, BELAGAVI.

Objective: To study the correlation of different phasesof Cerebral Visual Impairment(CVI) in children aged 1-4years and to correlate it with MRI.

Introduction: Your child/ward is being invited to participate in this study to correlate MRI of brain with phase of cerebral visual impairment in children with cerebral visual impairment.

Explanation of procedure: If, you agree for your child to be part of the research study, you will be asked the relevant history and your child/ward will be subjected to relevant clinical examination and investigations.

Withdrawal from participation in the study: Participation in this study is voluntary. You will be free to decide whether your child will participate in this study or continue participation once enrolled. In case you decide to withdraw your child's participation, you are free to do so. However, please convey the decision to the principal investigator.

Possible benefits from participating in the study: Your child/ward will not get any benefits by participating in this study. The data gathered will help the population at large.

Possible risks from participating in the study: There are no risks involved in participating in this study.

Privacy and confidentiality: The information collected from you will be coded, to prevent any person from identifying your child. Your identity will never be revealed. The data collected from you will be kept confidential and only processed or aggregated data will be used for publication.

Financial incentives: You will not receive any payment for participating in this study.

Authorization for publication of aggregated data: Results obtained after processing of the aggregated data will be published for scientific purposes and or presented to scientific groups. However, your identity will never be revealed.

Questions: In case of any questions with regard to this study, you are free to contact: "……..." If you have any question or complaints with regard to your right as study participant you may contact "Dr Harsha Hegde, Chairperson, Ethical committee of JNMC, 0831-2473777 Extension 4052."

Legal rights: By signing this consent form, we are not waiving any of your legal rights.

CONSENT STATEMENT

I am making a voluntary decision for my child to participate in the study "CORRELATION OF DIFFERENT PHASES OF CVI IN CHILDREN AGED 1 TO 4 YEARS WITH MRI : A ONE YEAR CROSS SECTIONAL STUDY AT KLES DR. PRABHAKAR KORE HOSPITAL AND MEDICAL RESEARCH CENTRE ". My signature below indicates that I have decided for my child to participate and I have read the information provided above or the information provided above has been read to me in the language that I understand best. I was given the opportunity to ask questions and that they have been answered to my satisfaction.

Signature or left thumb impression of the authorized representative/ parent:

Name of the authorized representative/ parent:

Relation to the subject:

Signature or left thumb impression of the witness:

Name of the witness:

Signature of the investigator:

Name of the investigator:

DATE:
PLACE:

ANNEXURE-III

PROFORMA

CORRELATION OF MRI WITH DIFFERENT PHASES OF CVI IN CHILDREN AGED 1 TO 4 YEARS : A ONE YEAR CROSS SECTIONAL STUDY

HOSPITAL ID: DATE:
NAME OF SUBJECT: AGE/ SEX:
ADDRESS: PHONE NO:

CHIEF COMPLAINTS:

1) Is there a colour preference Yes / No
2) Difficulty in finding thing/toys in complex environment Yes / No
3) Better vision for movement at near/far objects Yes / No
4) Longer time to find and recognise (i.e.Visual latency) Yes / No
5) Difficulty in visualising objects at distance **>**1to 2 feet Yes / No
6) Gaze preference/light gazing Yes / No
7) Visual field preference Left/Right /Centre/Upper/Lower
8) Difficulty in visualsizing in new surroundings Yes / No
9) Does the child blink to touch/threat(Visual reflex) Yes / No
10) Does the child look and reach for objects(Visual guided reach) Present/Absent

BIRTH HISTORY: Antenatal -
Gestational Period - _____Weeks Preterm / Term
Birth Weight - _____ Grams
DELIVERY Normal / Forceps / C-Section
CRY- Immediate / Delayed
HISTORY OF:

- oxygen therapy Yes / No
- Neonatal jaundice Yes / No
- Convulsions Yes / No
- Documented hypoglycemia Yes / No
- Chorio amniotism Yes / No

MILESTONES: Normal / Delayed
FAMILY HISTORY:
CONSANGUINITY: Absent / Present
CNS- Cerebral Palsy / Global Developmental Delay / Autism

OCULAR EXAMINATION

Orthophoria / Esotropia / Exotropia

Anterior Segment

Posterior Segment

Nystagmus- present/absent

Vision with TAC

	Right Eye			**Left Eye**		
	AT 38cm	**55 cm**	**84 cm**	**38 cm**	**55 cm**	**84 cm**
OBSERVATION						

Refractive Error- None/ Myopia/ Hypermetropia/ Astigmatism

CVI PHASE: Phase I / Phase II / Phase III

RATING 1: CVI range
RATING 2: Total score

Paediatric Diagnosis (etiological):

MRI SCORING: (0 = no abnormality 1 = abnormality seen)

For each lobe cortical grey matter and subcortical white matter were scored.
Thalamus and basal ganglia were coded and summed for striatum score.
The left, right hemisphere and vermis of the cerebellum were coded
In the visual pathway 3 regions were considered: pregeniculate, postgeniculate area and visual cortex

TOTAL

RIGHT HEMISPHERE

1. Lobe involved: RIGHT HEMISPHERE [0-10]
   - 1) Frontal[0-2] ☐
   - 2) Parietal[0-2] ☐
   - 3) Occipital[0-2] ☐
   - 4) Temporal[0-2] ☐
   - 5)Striatum[0-2] ☐

RIGHT ☐

LEFT HEMISPHERE

2. Lobe involved: LEFTT HEMISPHERE [0-10]
   - 1) Frontal[0-2] ☐
   - 2) Parietal[0-2] ☐
   - 3) Occipital[0-2] ☐
   - 4) Temporal[0-2] ☐
   - 5)Striatum[0-2] ☐

LEFT ☐

3.	BRAINSTEM		[0-1]	
4.	CEREBELLUM	1) Left Hemisphere	[0-1]	
		2) Right Hemisphere	[0-1]	
		3) Vermis	[0-1]	
5.	VISUAL PATHWAY SCORING	1)Pregeniculate area	[0-1]	
		2)Postgeniculate area	[0-1]	
		3)Visual Cortex	[0-1]	
		TOTAL MRI SCORING [OUT OF 27]		

NAME OF THE INVESTIGATOR : SIGNATURE - _____.

NAME OF THE GUIDE : SIGNATURE - _____.

ANNEXURE IV–PHOTOGRAPHS

Photograph 4 : ANTERIOR SEGMENT EXAMINATION

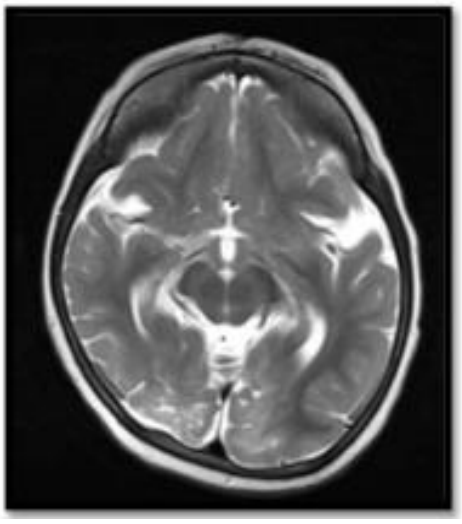
Photograph 5 :RESPONSE TO TOUCH AND THREAT

Photograph 6: FIXATION AND COLOUR PREFERENCE

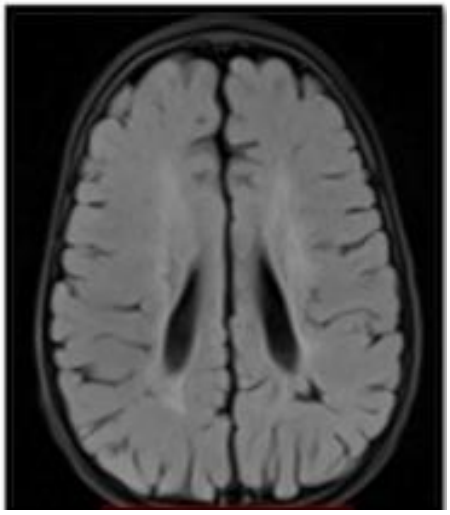
Photograph 7 :DILATED RETINOSCOPY

Photograph 8:DILATED FUNDOSCOPY FOR OPTIC NERVE HEAD EVALUATION

Photograph 9 :MRI BRAIN



HIE



PVL

ANNEXURE-V

KEY TO MASTERCHART

B. Wt.	:	birth weight
Y	:	Yes
N	:	No
M	:	Male
F	:	Female :
PT	:	Pre- term
T	:	Term
-	:	Absent
+	:	Present
LSCS	:	Lower- segment cesarean section
NVD	:	Normal vaginal delivery
WNL	:	Within normal limits
GDD	:	global developmental delay
CP	:	cerebral palsy

S.No.	NAME	Age	SEX	COMPLAINT (X/10)	Term/pre- term	B.Wt. (grams)	delivery	nicu admission	oxygen therapy	jaundice	convulsions	Hypoglycemia	chorioamniotion	milestones	consanguinity	ant segment	post segment	nystagmus	vision with TAC(cy/cm)	refraction	cvi phase	paediatric diagnosis	right hemisphere(lobes involved)	right hemisphere(MRI score)	Left hemisphere(lobes involved)	left hemisphere(MRI score)	brainstem	cerebellum	visual pathway	total MRI score	temporal lobe	parietal lobe	occipital lobe
1	Aliahmad	2	M	6	T	2700	LSCS	-	N	N	N	N	N	delayed	+	epicanthal fold +	small heperopic disc	+	0.64	hypermetropia	iii	neurodegenerative disorder						3				3			
2	Umair	2	M	3	PT	2000	LSCS	+	Y	Y	Y	Y	N	delayed	-	orthophoria	large pale cup	-	19	None	ii	GDD	occipital	1	occipital	1			1	3			2
3	Manu	1.5	M	5	T	2700	LSCS	+	Y	N	Y	Y	N	delayed	-	esotropia	mild temporal pallor	-	0.23	None	i	GDD	parieto-occipital	3	parieto-occipital	3			1	7		2	4
4	vaibhav	1	M	4	PT	2400	LSCS	+	Y	Y	Y	N	N	delayed	-	alternating exotropia	b/l temporal pallor	-	0.32	hypermetropia	i	dyskinetic CP	parietal	1	parietal	1				2		2	
5	dhanvin	2.5	M	7	PT	3700	LSCS	+	Y	N	N	N	N	delayed	-	orthophoria	temporal pallor with large disc	-	0.86	myopia	iii	GDD							1	1			
6	prutvik	1	M	5	PT	2040	LSCS	+	N	Y	N	N	N	delayed	+	orthophoria	small oval disc	+	0.23	hypermetropia	i	spastic CP	frontal	2	frontal	2		3		7			
7	tejas	1	M	5	T	2700	NVD	+	N	Y	Y	Y	N	delayed	-	orthophoria	WNL	-	0.64	None	i	GDD	pareito-occipital	2	pareito-occipital	2				4		2	2
8	sahil	4	M	2	PT	1500	NVD	+	N	Y	N	N	N	delayed	-	orthophoria	WNL	-	9.8	None	iii	spastic CP	parietal	1	pareital	1				2		2	
9	spoorthi	4	F	9	T	2800	NVD	+	Y	Y	N	N	N	delayed	-	orthophoria	WNL	-	6.5	myopia	ii	dyskinetic CP	parietal-stratum	2	pareital-straitum	2				4		2	
10	prathmesh	2	M	4	T	3100	NVD	+	Y	Y	Y	N	N	delayed	-	orthophoria	WNL	-	6.5	None	ii	infantile seizures	temporal	1	temporal	1				2	2		
11	parvati	1.5	F	3	T	2400	NVD	+	Y	N	Y	N	N	delayed	-	orthophoria	WNL	+	6.5	None	iii	dyskinetic CP with GDD						1		1			
12	nandish	1.5	M	3	T	2800	NVD	-	Y	Y	Y	N	N	delayed	-	infantile esophoria	large disc, temporal pallor	+	1.3	hypermetropia	i	dyskinetic CP with GDD	straitum	1	straitum	1			1	3			
13	mukund	3	M	9	T	2700	LSCS	-	N	N	N	N	N	delayed	-	exotropia	WNL	-	0.23	hypermetropia	iii	GDD	fronto- pareito-occipito-temporal	4	fronto- pareito-occipito-temporal	4			1	8	2	2	2
14	shreyas	4	M	4	T	3500	LSCS	-	N	N	N	N	N	delayed	-	alternating exotropia	WNL	-	0.43	astigmatism	ii	dyskinetic CP								0			
15	laxmi	1	F	4	PT	2500	NVD	+	N	Y	Y	Y	N	delayed	+	orthophoria	WNL	-	4.8	None	ii	GDD			fronto- pareito-occipito-temporal	4			1	5	1	1	1
16	shiva	1	M	7	T	2500	LSCS	+	Y	N	N	N	N	delayed	-	orthophoria	optic nerve hypoplasia	-	0.23	hypermetropia	i	GDD	fronto- pareito-occipito-temporal	4	fronto- pareito-temporal-straitum	4			1	9	2	2	1
17	taifur	1	M	6	T	2500	NVD	+	Y	N	Y	N	N	delayed	-	orthophoria	clinically oval disc	+	0.23	myopia	i	IESS with spastic quadriparesis	fronto- pareito-occipito-temporal	4	fronto- pareito-occipito-temporal	4				8	2	2	2
18	zebadiah	1.5	M	2	T	2700	LSCS	+	N	N	Y	Y	N	delayed	-	orthophoria	b/l optic nerve hypoplasia	-	4.8	hypermetropia	ii	spastic CP	parieto-occipital	4	parieto-occipital	4				8		4	4
19	nida	1.5	F	6	T	2900	NVD	+	Y	N	Y	Y	N	delayed	-	estropia	small oval pale disc	-	1.6	None	i	neonatal hypoglycemic brain injury	occipital	2	occipital	2			1	5			4
20	samarth	1	M	2	T	2500	NVD	+	Y	N	Y	Y	N	delayed	-	alternating exotropia	small vertically ovaldisc	-	0.43	hypermetropia	i	hypocalcemia with seizures	fronto- pareito-temporal	3	parieto -temporal	2				5	2	2	
21	manvita	5	F	6	T	2400	NVD	-	N	N	N	N	N	delayed	+	orthophoria	pale disc?optic atrophy	+	0.23	None	i	dyskinetic CP	parieto-ocipito-temporal	3	pareito-occipito-temporal	3			1	7	2	2	2
22	diya	1.5	F	5	T	1900	NVD	+	N	N	N	Y	N	delayed	-	orthophoria	WNL	-	6.5	None	i	GDD	parieto-occipital	2	parieto-occipital	2			1	5		2	2
23	pradeep	4	M	4	T	2300	NVD	-	N	N	N	N	N	delayed	+	orthophoria	WNL	+	9.8	myopia	ii	hemiparalytic cp	parieto-occipital	2	parieto-occipital	2				4		2	2
24	sambhavam	1	M	3	T	2000	LSCS	+	Y	Y	Y	Y	N	delayed	+	orthophoria	pale disc,double ring sign	-	0.23	hypermetropia	i	spastic CP	parieto-occipital	2	parieto-occipital	2			1	5		2	2
25	deeksha	4	F	3	T	3500	LSCS	-	N	N	N	N	N	normal	+	alternating exotropia	WNL	-	0.64	None	i	GDD	fronto-parieto-occipital	3	fronto-parieto-occipital	3			1	7		2	2
26	kiran	2.9	M	5	T	2100	NVD	-	N	N	N	N	N	delayed	-	orthophoria	optic nerve hypoplasia	-	0.23	None	i	dyskinetic CP	parieto-occipital	2	parieto-occipital	2			1	5		2	2
27	ayan	2	M	6	T	2500	LSCS	+	N	Y	Y	N	N	delayed	+	exotropia	pale large tilted disc	+	0.23	None	i	dyskinetic CP	parietal	2	parietal	2				4		4	
28	vishwanath	2	M	5	T	2750	NVD	+	Y	Y	N	N	N	delayed	+	orthophoria	WNL	-	6.5	None	iii	dyskinetic CP								0			
29	vedanth	4	M	5	T	3000	LSCS	+	Y	N	Y	N	N	delayed	-	orthophoria	WNL	-	6.5	None	iii	GDD	fronto-parietal	2	fronto-parietal	2				4		2	
30	gautami	2	F	5	T	2550	NVD	-	N	N	N	N	N	delayed	+	convergence spasms	mild temporal pallor	-	0.23	None	ii	GDD	fronto- pareito-temporal	3	fronto- pareito-temporal	3			1	6	2	2	
31	dhruv	1.5	M	6	T	3700	LSCS	+	Y	Y	N	N	N	delayed	-	orthophoria	WNL	+	0.32	None	i	GDD	parieto-occipital	3	parieto-occipital	3			1	7		4	2
32	abhishek	2.5	M	7	PT	1900	NVD	+	N	Y	Y	N	N	delayed	-	orthophoria	WNL	-	0.23	None	i	dyskinetic cp with microcephaly	fronto-parieto-occipital	3	fronto-parieto-occipital	3			1	7		2	2
33	amresh	4	M	4	T	1000	NVD	+	Y	Y	Y	N	N	delayed	-	both eye pseudophakia	WNL	-	0.23	None	iii	CP	parietal	1	parietal	1				4		2	
34	sanchrit	3	M	2	T	2700	NVD	+	Y	N	Y	N	N	delayed	-	alternating exsophoria	mild temporal pallor	-	4.8	hypermetropia	ii	GDD	fronto- pareito-occipito-temporal	4	fronto- pareito-occipito-temporal	4				8	2	2	2
35	hanmant	2	M	4	T	2075	LSCS	+	Y	N	Y	N	N	delayed	-	orthophoria	WNL	-	0.23	astigmatism	ii	dyskinetic cp with microcephaly	parieto-occipital	2	parieto-occipital	2				4		2	2