"ROLE OF MAGNETIC RESONANCE IMAGING IN EVALUATION OF CHILDREN WITH DEVELOPMENTAL DELAY - A ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY."

BY

REG NO. BS0119005

Dissertation

Submitted to
KAHER, Belagavi, Karnataka,
In partial fulfilment of the requirements for the degree of

M.D.

In

RADIO-DIAGNOSIS

DEPARTMENT OF RADIO-DIAGNOSIS,
J. N. MEDICAL COLLEGE,
BELAGAVI -590010. KARNATAKA

APRIL - 2022

KLE ACADEMY OF HIGHER EDUCATION AND RESEARCH, BELAGAVI, KARNATAKA

Endorsement by the HOD/Principal/ Head of the Institution

This is to certify that the dissertation entitled **"ROLE OF MAGNETIC RESONANCE IMAGING OF BRAIN IN EVALUATION OF CHILDREN WITH GLOBAL DEVELOPMENTAL DELAY- ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY"** is a bonafide research work done by **(REG NO BS0119005).**

Dr. ASHWIN S. PATIL
M.D. RADIO-DIAGNOSIS

Professor and Head,
Department of Radio Diagnosis,
J. N. Medical College,
Nehru Nagar, Belagavi – 10

Date:

Place: Belagavi

Dr. N.S. MAHANTASHETTI
M. D. PEDIATRICS

Principal,
J. N. Medical College,
Nehru Nagar, Belagavi – 10

Date:

Place: Belagavi

PALGIARISM CERTIFICATE

KLE JAWAHARLAL NEHRU MEDICAL COLLEGE
(Recognized by Medical Council of India, New Delhi)
Accredited 'A' Grade by NAAC (2nd Cycle) Placed in Category 'A' by MHRD (GoI)
Nehru Nagar, Belagavi- 590 010, Karnataka, INDIA
0831 - 2474330 0831 - 2470389 www.jnmc.edu principal@jnmc.edu

Ref No: MDC/PG/ Date: 25-11-2021.

ACCEPTANCE LETTER

The softcopy of thesis entitled: "**ROLE OF MAGNETIC RESONANCE IMAGING OF BRAIN IN EVALUATION OF CHILDREN WITH GLOBAL DEVELOPMENTAL DELAY – ONE YEAR HOSPITAL BASED CROSS- SECTIONAL STUDY**" has been submitted for Anti-Plagiarism check through Turnitin software. The scan has been carried out and the scanned output reveals a match percentage of 05% which is within the acceptable limits of 10% as per the guidelines given by UGC.

Guide.

Dr. (Mrs.) N.S. Mahantashetti.
Chairperson-Anti-plagiarism Committee &
Principal,
J. N. Medical College, Belagavi.

To,
Reg. No. BS0119005.
Postgraduate Student,
2019-20 Batch,
Department of RadioDiagnosis,
J. N. Medical College, Belagavi.

LIST OF ABBREVIATIONS:

DD	Developmental delay
GDD	Global developmental Delay
MRI	Magnetic resonance Imaging
PVL	Periventricular Leucomalacia
MRS	Magnetic Resonance Spectroscopy
DDST	Denver Developmental Screening Test
ID	Intellectual disability
CST	Caregiver Skills Training Program
WHO	World health organization
DCHS	Drakenstein Child Health Study
CMV	Cytomegalovirus
HIE	Hypoxic ischemic encephalopathy
WM	White matter
CC	Corpus callosum
NAA	N-acetylaspartate
DTI	Diffusion tensor imaging

Cho	Choline
Cr	Creatinine
LSCS	Low section cesarean section
NICU	Neonatal intensive care unit
VR	Virchow robin
ADC	Apparent diffusion coefficient
MPRAGE	Magnetization Prepared Rapid Gradient Echo Imaging
SWI	Susceptibility weighted images
DWI	Diffusion weighted images

ABSTRACT

BACKGROUND:

Developmental delay is a common socioeconomic problem among children. According to recent study done by WHO about 5% of children under 14 years have some or the other type of developmental delay or childhood disability. The prevalence of developmental delay in India under the age of 2 years is approximately 2%.

MR imaging has played dominant role in the exhaustive assessment of children with DD, since many specified patho-physiological and etiological causes which could be leading to developmental delay could be easily identified.

Global developmental delay is subtype of developmental disorder. It is described as developmental delay well below the specific standard deviation in two or more domains. Developmental delay could happen due to progressive or static disorder of the central nervous system. Stability , regression, or disease progression can develop in patients with these disorders. The major causes of global developmental delay included a variety of diseases, large number of which are associated with particular abnormalities in MRI brain.

Neuro-imaging helps in laying out the important details as evidences of old hypoxic insult, / traumatic injury or specific abnormality that could point to a particular disease or a group of diseases

The aim of this study is to access the role of MRI n in evaluation of children with developmental delay.

MATERIALS AND METHODS:

One year prospective cross sectional study was done in Department of Radio-diagnosis at the KLE'S Dr Prabhakar Kore Hospital & MRC, Belagavi.

85 patients were included in the study through universal sampling. The patients were subjected to MRI brain scan .

The study population were analysed based on age , gender, clinical history, head size, consanguineous marriage, abnormalities on MRI , etiological cause of developmental delay and spectroscopy findings.

RESULTS:

The most common cause of developmental delay was congenital/ developmental anomalies (25.88%) , with the second highest cause being Traumatic/ Neurovascular diseases (18.82%) and metabolic causes(18.82%).

More than 72.94 % of the children were clinically diagnosed to have cerebral palsy with more than 72% of them showing abnormal MRI findings.

MRI showed high yield with92.9 % of the patients showing abnormal MRI findings out of which white matter, corpus callosal and ventricular abnormalities were most common.

Yield of MRI was higher with eventful birth history with about 70 % of the children with LSCS delivery , 89% of the children with low birth weight, 80% of the children with pre term delivery, 71% of the children with hypoxic insult and 90% of the children with NICU admission showing abnormal MRI findings,

75 % of the children with microcephaly and 60% of the children with macrocephaly had abnormal MRI findings.

INTERPRETATION AND CONCLUSION:

Global developmental delay is a common condition. In our study majority(69.41%) of the study population were females and majority aged 1-3 years . MRI showed high utility with 92.9 % of the subjects showing abnormal MRI brain findings with most common abnormality being in white matter , corpus callosum and ventricles.

This study highlighted the role of MRI to guide the clinician towards the cause. MRI was able to diagnose large majority of children with congenital/Developmental anomaly(25.88) and hypoxic ischemic insult(18.82%) , metabolic disorders (18.82%), infectious (3.5%) or neoplastic (1.2%) etiology.

The patients with DD and additional features had higher yield with 77.27% of theses patients showing abnormal MRI findings whereas 65.85% of the patients with only developmental delay showing abnormal MRI findings.

MRI brain is a reliable modality with high yield in evaluation of children with global developmental delay. It gives wide range of information which if used complementary to the clinical data can guide us to correct diagnosis and prognosticating the disease. Early diagnosis could aid in early initiation of treatment and better quality of life.

Keywords: Developmental delay, MR spectroscopy, MRI.

CONTENTS

LIST OF TABLES

LIST OF GRAPHS

LIST OF FIGURES

INTRODUCTION

Developmental delay is a common socioeconomic problem among children. According to recent study done by WHO about 5% of children under 14 years have some or the other type of developmental delay or childhood disability. The prevalence of developmental delay in India under the age of 2 years is approximately 2%[1] .Mostly they have mild delay but a small percentage of these children have shown to have severe psychomotor delay. With the current diagnostic methods, the reason of developmental delay (DD) is unknown frequently. families and clinicians could be discouraged by the lack of neuro-imaging association especially when taking into accountlong-term prognosis and therapeutic options.

MR imaging has played dominant role in the exhaustive assessment of children with DD, since many specified patho-physiological and etiological causes which could be leading to developmental delay could be easily identified. However, frequently the children with mild DD have normal MRI brain findings, and around 15% of the school-going children have shown to have some form of mild DD.

To detect the difference in brain metabolism in these children with DD of unidentified cause in whome no MRI abnormalities have been found, MR Spectroscopy and DTI could be used. These additional imaging studies could help to find the cause of the DD, and contribute to long term functional outcome for these children and hence could be included in the diagnostic algorithm of the neuro-radiological assessment.

AIMS AND OBJECTIVES

- **Primary objective:** To evaluate the yield of MRI in evaluation of children with global developmental delay.

- **Secondary Objective:** To determine role of newer sequences of MRI in evaluation of children with global developmental delay

REVIEW OF LITERATURE

Developmental delay –basics

Development is a continuous and complex process of maturation, which parallels growth of children. It starts from the conception time and continues uptill maturity and can affect many aspects.[1] An infant could demonstrate a wide variety of relations with the surrounding environment during the process of development. Unlike the sequence of development, the rate of developmental process ranges from one kid to another and it is seen to depend on various environment aspects such as chronic disease and genetic factors[2]. Global development in children is usually evaluated according to four aspects of fine motor, gross motor, social skills and language skills. The children who are unable to attain expected developmental skill at the appropriate age are in all domains considered to be suffering from Global Developmental Delay (GDD).

Global developmental delay is subtype of developmental disorder. It is described as developmental delay well below the specific standard deviation in two or more domains. Developmental delay could happen due to progressive or static disorder of the central nervous system. Stability ,regression, or disease progression can develop in patients with these disorders. The major causes of global developmental delay included a variety of diseases, large number of which are associated with particular abnormalities in MRI brain. Multiple methods and tests are there to assess the developmental delay. The widely popular examinations which are usually used is Denver Developmental Screening Test (DDST) and its altered form was the Denver Developmental Screening Test II (DDSTII)[3].

Only based on patient history and physical examination these causes cannot be found out; nevertheless, other studies like metabolic tests, genetic investigations, serological tests, and neuro-imaging were necessary for further investigation. Neuro-imaging helps in laying out the important details as evidences of old hypoxic insult, / traumatic injury or specific abnormality that could point to a particular disease or a group of diseases [1,4,5].

According to the number of domains affected, developmental delay is classified into three types: [6,7]

1. Isolated DD: only if its concerning a solitary domain
2. Multiple DD: if involving two or more domain or if its development lines are affected
3. GDD : if delay is present in all of the developmental subsets.

Other subtypes are:

Intellectual disability (ID) is a type of developmental disorder in which primarily the comprehensive function is affected. According to the American Association on Intellectual and Developmental Disabilities (ID) , it was attributed to the lifetime developmental lacunae in regions accountable for adaptive skills development , education, independence , problem-solving and generally have onset before 18 years.[7,8]

Developmental disorders are a huge collection of disorders in which, the classical sequence & the pattern of development is disturbed with delay in or/and deviation from the development process.[7] In spite of the policy of American Academy of

Pediatrics of timely screening, a large numeral of developmental disorders remained un-diagnosed and not treated**.** [9]

Developmetal delay –burden (global)

Salomone et al [10] in his study on Developmental disorders and delays done in 2019 said that globally, around 52,90,00,000 children under 5 years of age had developmental disabilities, for example sensory disablity, autism disorder and intellectual disability. Of these 52.9 million children, 95% of them reside in low-to-middle-economic countries since these children lacked access to health care. They also told about a novel Caregiver Skills Training Program (CST) developed by the WHO for the family of children with development disorders or to help delay or to decrease such treatment gap . The program was developed to help support the child's ,communication skills and adaptive behaviours to reduce the challenges of the disability.

Dornelas et al [11] ,based on literature review had build a conceptual map on neuro psycomotor developmental delay in 2015. In this literature search they found 10% of population of every country had a disability ,of one or another kind. According to the WHO, the exact prevalence of DD is unknown. Out of all these children 4.5% were younger than 5 years.

According to Vitrikas et al [12] in their study on when and how to screen DD children in 2017, they stated, roughly 15% children in US, were reported to have minimum single developmental problem. Out of these less than 1/5th of these children were able to receive earlier treatment before 3 years of age. They also suggested regular utilization of a well grounded screening tool at frequent intervals, together

with the medical general physician watching at out patient children visits, to get better chances of early discovery.

Km YS,[13] studied the prevalence of intellectual disability in children aged 7 to 12 years of age in south Korean community from special education schools with disability register and regular schools in September 2011 . The prevalence of autism spectrum disorder was found to be 2.64% , with 0.75 % being from the general population group and 1.89% being from the high probability group.

Hatton et al did a study on people with learning disabilities in England in 2013 . They mentioned that under age five children and adults, the prevalence of intellectual disability in children is 2.7% and 2.17%, respectively. In school-age or younger children the global developmental Delay incidence rate is 1% to 3% .[14]

Vitrikas et al [15] studied the prevalence of DD in different domains in children on the basis of information told from children who are getting services by USPSTF in the year 2007. The prevalence of DD in different domains in children was given as below:

- Cognitive Disability (8%)
- Language and Speech (2% - 19%)
- Cognitive (1% - 1.5%)
- Any other delay (15%)

Study done by Drakenstein Child Health Study (DCHS) in South Africa in the year 2019, stated that prevalence of DD was higher amongst boys in the high-risk environment . Similarly , few similar studies had also described somewhat higher

incidence in the males. This was hypothesized to be owing to genetic variability in the X chromosome.[8,16]

Meerding [17] performed a study in 1998 to determine the healthcare resource burden by different illnesses and their variations with sex and age by obtaining information of healthcare use from all the 22 healthcare sectors in Netherlands. They had determined that the lifetime cost (both direct and indirect) required to support children with considerable intellectual developmental delay exceeded to that of a patient amid cardiovascular and cancer diseases combined, approximately around $1 million for one person. The Cost was seen to increase slowly from childhood to adult life and was seen to reach peak tremendously from the age of 50 years till the oldest age group.

According to World health organization's report on disability done in Geneva, World bank in 2011, the global prevalence of developmental delay in children was 1 to 3%. In this world report it was also stated that approximately 15% out of worlds' population was living with some or the other form of disability.[18,3,6]

In the United States, under 18 years of age developmental or/and behavioral disorders occurred in 16-18% of the children.[19,20,21] The prevalence of childhood disability ranged from 15% in Pakistan and Jamaica and 8% in Bangladesh .[21]

Mackrides P S et al [19] had suggested the utilization of valid screening tools at regular and repeated interval, along with general physician surveillance, at out patient-children visits. The previous literature had supported screening for DD with several parent-completed tools than with directly administered tools. Most popular parent-completed tools were the Parents' Evaluation of Developmental Status and the

Ages and Stages Questionnaire. Opportunities for early intervention may be lost, if developmental delays are detected too late.

Boyle C [20] in their study done in 2011 had studied the trend in the occurrence of developmental disabilities in the US in children ageing from 3 - 17 years from the data derived from the 1997 to 2008 National Health Interview Surveys, which were nationally representative sample of almost all the US household. Developmental disabilities were frequent, were reported in one out of six children in the US from 2006 - 2008. Prevalence of the developmental disabilities had become greater than before from 12.84% - 15.04% over the time of 12 years. The percentage of children with selected developmental disabilities (attention deficit disorder, autism, and other developmental delay disorder) were also greater than before, hence requiring the need for more education and health solutions.

Newacheck P [21] in their study on Epidemiological profile of patients with special needs done in 1998 , had found out the connection between the health amenity expenditure for different special health care needs of the children and respective families' opinion on economic load. They used data from national survey of children with special health care needs and estimated relationship between perceived heal care burden in families and the heal care expenditure along with family control factors. Their analysis suggested that the health care expenditure for special needs infant was 250 dollar or more and is usually linked with the perception of high financial trouble on the family . Adding to that, families who belonged to inferior socioeconomic status, apparent economic burden was felt at much lesser level of expenditure. Hence, health care team who are treating these children with special

needs had a crucial role in assessing and understanding families financial pressure as a part of their health care delivery to a child.

Developmental delay-burden (India)

Singh et al [22] did a review on the determinants of developmental delay in children less than 5years of age in 2017. They found the prevalence of developmental delay ranged from 2.31% to 19.8% amongst under five children in India .

The cross sectional study was done by Nair et al [23] in 2009 to determine the prevalence of developmental delay, disability and deformity in 0 to 5 years aged children who were selected randomly from a particular block in Alappuzha District of Kerala in India. Out of the total 12, 520 children under 5 years in that chunk, there were approximately 311 children with developmental delay, giving an approximate prevalence of 2.5 %. The prevalence upto 2 years came out to be 2.31 (95 % CI, 1.91 to .71) and from 2 to 5 years it was 2.62 % (95 % CI, 2.25 to 2.99).

Jacob et al [24] conducted a study in 2013 to study the development of a child of an average migrant construction workers who were visiting the Mumbai Mobile Creches daycare centres and also to identify children who could be at risk of having developmental delay .792 children were screened using a psychosocial screening test developed by Indian Council of Medical Research (ICMR). The five areas of development, namely vision , fine motor, gross motor, conceptual development , social skills ,personal skills and hearing language were measured using this test. Results of the study had indicated that 91 per cent of the children children were able to attain developmental milestones on time. The prevalence of developmental delay was found to be 9 per cent. Out of the total 792 children the 2 % of the children who

were falling between the 95th to 99th percentiles were reported to have "risk" , who needed intervention as soon as possible to prevent developmental delay . Younger kids were seen to be more prone to develop developmental delay. In the study, they also emphasized the necessity of regular assessment of developmental of migrant children and the importance of earliest intervention when any kind of delay is suspected.

Ali et al [25] had conducted a cross sectional study in 2011 to assess the Global Developmental delay and growth and also the various predisposing factors amongst the children aged 3 years who are residing in the rural communities of India. In this study, about 530 children were studied for three years to assess their developmental and growth delay. This study found high prevalence of DD in rural population and poor child heal in these regions compared to the rest (19.8%). This was due to usage of a different tool for assessing and also due to difference in the community setting. The children were assessed by administering The Ages and Stages Questionnaire (ASQ) to the mothers by a trained interviewers. Children displayed delay in gross motor (38.1.1%), personal-social (42.5%), and problem solving skills (34.9%). The educational level of the mother was seen to be associated with problem solving skills and communication positively (P=0.000) whereas the household income per month was seen to be associated with problem-solving skills, gross motor and communication (positively p=0.000).

Vora et al [26] in 2013 studied 200 children under two year of age attending the health center using TDSC and found the prevalence of Developmental Delay to be 9.5%. . 181 out of 200 children had normal development and only 19 children (5.8-14.4) % showed delay.

Meenai et al [27] in 2009 studied the prevalence of developmental delay in north India , Haryana which was similar to prevalence in rest of regions in India. Prevalence was observed in 6.3 % of the children. Overall about 221 children who aged 4 to 18 months were incorporated in this research. The prevalence of the gross motor milestone achievement for each one of the six milestones ranged from 91.6% - 98.4% in this study. The mean age of motor development a 0.1–2.1 month delay compared to the WHO mean age of motor milestone achievement. After adjusting the various variables, the children who were second birth order or more were associated with timely achievement of the gross motor milestones.

Routray et al [28] in 2019 conducted a study among children living in an orphanage in Odisha and found a very high prevalence (52.1%) of developmental delay as compared to other studies. Also in another study conducted by him, it was found that in comparison to children living in a slum the prevalence of global developmental delay amongt children living in an orphanage was much higher (13.7% Vs 37%) .

ETIOLOGY

Developmental delay has multi-factorial etiology. The etiological cause for the bulk of cases of developmental delay is thought to be idiopathic. If recognized, etiologies could be psychological, genetic and /or environmental factors.

Singh et al [22] in their study, they also showcased that a child's development is inter play between environmental and genetic factors. Low birth weight, artificial feeding, high birth order, , children with PEM, working mother/single mother, diarrhea etc are found to be associated with developmental delay in children less than

five years along with other contributing factors such as overcrowding, poverty, substandard housing, etc. They suggested in their study that developmental delays and risk factors associated with it should be included in office practice and appropriate norm based screening tools should be incorporated for earlier recognition of developmental delay.

Genetic: As per now**,** for developmental delay there is not a known genetic substrate. But, the developmental patterns have been seen to be more often familial, (including the late onset of talking and walking . In spite of that, the developmental delays could also be representing risks for developmental disorders or syndromes . There has been a sizeable variations in genetics of the developmental disorders, ranges from duplications , deletions , insertions and copy number variants (CNV's). While mostly they could be rare variants, few of them might represent common variants. The Fragile X syndrome which is a trinucleotide repeat disorder (CGG) is the common genetic feature known, for ID(intellectual diability)which targets the Fragile Mental Retardation 1 (FMR1) gene situated at the X-chromosome. Fragile X has been shown to increase risk factor for Atrial Septal Defect as also.Inthe cases of Prader-Willi and Angelman syndromes, imprinting could also be seen, which could vary with the paternal and the maternal loss of functionality on the chromosome 15q. they also suggested that , physical phenotypes and developmental delay could be associated with other disorders which have oe or more extra chromosomes or pieces of chromosomes, for instance, Patau Syndrome, Down syndrome (Trisomy 21) and Edward Syndrome.[29][30][31][32] Other disorders which are X-linked included Rett Syndrome in females and coffin-Lowry syndrome predominantly in males .[8]

Environmental: An extensive variety of environmental factors could be leading to developmental delay and subsequently leading to developmental disorders. These environmental factors could be affecting the developmental process at one single or numerous points in the course of development.

Antenatal:

- Heritable disorders, for instance Down syndrome , Fragile X syndrome or chromosom duplications & microdeletions.
- Primigravida
- Poverty
- Maternal infections like toxoplasmosis, rubella and cytomegalovirus (CMV).
- Short inter-pregnancy interval
- Iunfections occurring in late maternity like HIV, varicella, malaria, etc.
- Teen pregnancy
- Prescribed medications such as cytotoxic or antiepileptic drugs (AEDs)
- Vascular causes like occlusion and hemorrhage
- Toxins /Teratogens including smoking, opioids , alcohol etc.

Perinatal:

- Poverty
- Metabolic — Hypoglycemia, bilirubin-related neurotoxicity
- Periventricular leukomalacia, Intrauterine growth restriction and premature birth
- Perinatal asphyxia, Hypoxic-ischemic injury, etc.

Postnatal:

- Poverty
- Infections for example neonatal meningitis or encephalitis
- Various metabolic disorders such as hypovolemia, hypoglycemia or hyponatremia
- Multivitamins, minerals deficiency or malnutrition due to iron, folate, Vitamin D, calcium deficiency
- Trauma — head trauma
- Inborn errors of metabolism - PKU
- Domestic violence, maltreatmentor/ and intimate partner
- Facors causing maternal stress like depression, anxiety etc.
- Various teratogens or toxins such as mercury, lead or arsenic etc.[7,16,33]

PATHOPHYSIOLOGY

Except for specific syndromes which are included in developmental delay, a large number of developmental delay cases are considered to be idiopathic. The underlying patho-physiology exactly is usually not known. Numerous mechanisms had been suggested in the past by various epidemiological studies which could be leading to developmental delay or disorder. Because few forms of developmental delay have been seen to be running in the families, various genes are assumed to be playing important role in the developmental delay process.

Large quantity of various mechanisms and genes have been proposed for the genetic transmission. Whilst, on one hand some other causes of developmental delay have known genetic etiologies like Down syndrome or Fragile X , for most others on the other hand, it is not clear. Some well-described disorders for example autism

spectrum disorder, more than 100 risk alleles have been defined. Poverty, profound deprivation and perinatal complications, along with other environmental stressors, could be playing a major part in causing developmental delay, however a specific causal links remains difficult.

In progenies, the normal control of the stress response has been done by the hypothalamic-pituitary axis (*HPA*). Few factors like modification of HPA ,psychosocial stressors during pregnancy and maternal immune activation (*MIA*), could be significantly affecting the fetal brain development, however, there have been no specification of a cause and effect relationships shown for the majority of the other disorder.

Boyce et al [35] in 2011 had suggested the concept of differential susceptibility. The study had suggested that there is increased risk of developing developmental anomalies by various number of factors which could generate a biological susceptibility by the environmental stresses , however were expressed only if the environmental stress had occurred. More so, even children who are vulnerable could be doing well if the environmental conditions were highly encouraging to development of resistance.

In a review done by Srour M [36] from the period of 1994 to 2004, about 261 children who were less than 5 years of age were referred for global developmental delay(GDD) assessment. Children who came for second opinion or with a known diagnosis of autism disorder or were excluded from this study. Patients who had specific physical signs like microcephaly, asymmetry or past history of perinatal asphyxia went through imaging; out of these, most of these children also undertook fragile X testing and karyotyping. A specific cause of global developmental delay

(GDD) was found out in 38% of the children out of which intrapartum asphyxia, chromosomal anomalies, cerebral dysgenesis, psychosocial deprivation , genetic syndromes fetal alcohol syndrome (6%) and term periventricular leukomalacia were the most common etiological causes. Various clinical features which were seen to be associated with identified etiologies included dysmorphic features, abnormal pre or peri-natal history microcephaly and atypical neurological examination. Amongst the children not having these clinical features, screening tests were able to reveal an etiology in few of the patients. An underlying etiology was only found out in about 50% of the children without having autistic features. [36]

MRI IN GLOBAL DEVLEOPMENTAL DELAY

Developmental delay usually presents with a broad variety of clinical and MRI findings spanning from being normal to having large number of abnormalities .Previous studies have been able to demonstrate different morphological appearances in children having developmental delay on MRI. Most commonly affected age group was <1 year of age. White matter was most commonly affected among all the anatomical structures and the most common cause was found to be neurovascular disease in which all cases of HIE were included .[37]

Brain development is believed to begin at conception and continue up till adulthood. The major embryological events in brain development usually begins with neurulation, neuronal proliferation and neuronal migration. The initial steps of operculization, gyral and sulcul development, and the myelination all take place, between the weeks 11 of gestation age and birth.

Errors in neurulation could result in a spectrum of congenital anomalies. The most severe end of the spectrum being anencephaly (that is complete absence of cerebral hemisphere) which is usually due to failure of closure of the anterior neurospore. Whereas, incomplete closure of the posterior neurospore could result in development of spina bifida. Myelomeningocele could develop if the neuroectoderm fails to separate completely from the cutaneous ectoderm. Chiari 2 malformation could result due to abnormality in neurulation of the hindbrain.

Errors in histogenesis and differentiation results in a number of embryonal neoplasms, such as medulloblastoma or primitive neuroectoderm tumors. malformations of cortical development could develop due to problems with NSC proliferation and differentiation.

Errors in neuronal migration and cortical development results mainly in malformation of cortical development.

Anomalies in sulcation and gyration lead to developmental errors in operculation, sucation and gyration. Microcephaly with simplified gyri patterns and micro-lissencephaly are few of two of the few representative anomalies that have lesser number of gyri and abnormal shallow sulci.

Since it's a continuous phenomenon, multiple factors affecting the process can have adverse effect in the form of developmental delay. Hence, developmental delay is not considered a diagnosis, however more of a clinical presentation. Multiple etiological factors like environment, nutritional ,traumatic ,infections, toxins, chronic disease and genetic factors play a role in this[38,39]. Hence vigourous investigation and evaluation can tell the reason of the developmental delay and help in streamlined cure

of treatable causes. Previous studies have revealed a cause of developmental delay in 65-85% of the patients[28,3,40,41,42,43]. Wide variation was attributed to different patient section in different patients. In patients, in whome clinical diagnosis was evident MRI Brain may not be advised. The yield of MRI in diagnosing anomaly is higher if novel techniques are used ,also if the study population selected has specifically more clinical features [43].

A study done on 81 children by Ali et al in Deccan college of medical sciences, Hyderabad, India in 2015 [44] could show the different morphological appearance of DD on MRI and additionally categorized them into different sub-groups. MRI was normal in 32% of the cases and 68% of them had abnormal MRI findings. The proportion of Traumatic/ Neurovascular Diseases were seen to be the etiology in majory of children (31%) with , Congenital & Developmental (17%) and Metabolic and Degenerative causes (10%) being the next highest cause.

A similar study done by Roshan et al in 2012[41] studied the underlying etiology in 105 patients with developmental delay . 71.8 % of the children had an underlying etiology. The fundamental etiology was determined in 71.8% of the children. Positive peri-natal history (p=0.039), abnormal MRI (p=0.001), and abnormal neurological examination had a significant higher rate of detection of etiology. The white matter and the ventricles along with the corpus callosum were seen to be the most commonly affected structures. 68% was the diagnostic yield in these patients and even superior yield was noted in children who present with DD and other signs and symptoms. They suggested that serial and sequential MRI may be beneficial in monitoring the progression of the disease.

GREY MATTER

Cortex formation disorders have structural abnormality of cerebral cortex. They are caused by loss of function of a gene (due to ischemia or infection) or by production of any abnormal gene responsible for normal development of cerebral cortex. Various classification systems have been described for cortical formation disorders. All these disorders can occur either during stage of proliferation, stage of migration, or stage of organization of the cortex. The wide variation in clinical presentation depends to a great extent on the stage of the arrest. Cortical formation disorders are thus one of the most important causes of developmental delay and epilepsy. MR imaging has shown to be an important instrument to diagnose these disorders.[45]

In the premature infants (extremely low birth weights)study group, an abnormality known as 'moderate-to-severe gyral maturational delay' , emerged as the only major predictor of the overall neuro-developmental impairment. Gyral maturation delay has also known to predict cognitive delay in children. So when diffuse cystic abnormality and gyral maturational delay and found, often impairments in development was as well. However, both predictors(diffuse cystic abnormality and gyral maturational delay) comparatively had lower sensitivity (30% to 67%), demonstrating that the absence of diffuse cystic abnormality as well as gyral maturational delay doesn't always mean impairment is absent as well.[46]

WHITE MATTER

Widjaja E Et al [43] conducted a in his study on 90 children about abnormalities of white matter among children having Idiopathic Developmental Delay

done in 2008. They had hypothesized that global developmental delay in children is due to abnormal white matter development that could further lead to structural changes which can be seen on MRI. He concluded that ventricular and corpus callosum abnormalities were seen among majority of patients having Idiopathic developmental delay , which indirectly indicates changes in the white matter . 11% out of these 90 were referred in view of DD alone, while 89% were referred in view of DD along with additional clinical features like seizures , abnormal head size and neurological deficit. Out of these 90 children 84% had abnormal MRI rest had normal. Abnormality in ventricles were seen in 48% ,corpus callosum abnormality in 44 %,white matter abnormality in 26%, hippocampi in 6%, cerebellum in, 6%, and brainstem in 4%. It was also suggested that further studies such as diffusion tensor imaging and quantitative methods are usually necessary with the use of evaluating white matter in these children.

As it is known that white matter development continues upto postnatal period, it was hypothesised that there would be abnormal development of white matter in idiopathic DD. It was shown by Pujol et al [46] in 2004 that decrease in myelinated white matter volume was associated with DD in children. They also demonstrated that asymmetries in the hemispheres were more in myelinated white matter compared rest of the cerebrum and had a higher probability to occur in patients with developmental delay compared to control subjects.

Paus et al,van der Knaap et al and Yakovlev and Lecours had suggested in their respective studies on post-mortem myelin staining conducted in feb2001, 1991, 2016 respectively stated that myelinated white matter indicates functional brain maturation [47, 48, 49]. Assessment of myelination helps to (a) determine the stage of

maturation a paediatric patient's brain (b)determine any possibility of delay during early infancy ;whereas behavioral milestones parallel stages of regional myelin deposition {Bird et al (1998), Barkovich et al.(1988) ; Dietrich et al (1987); McArdle et al (1987); Staudt et al (2000)}[50, 51, 52, 53, 54] . In spite of that, at two years of age, a child's brain starts showing appearance similar to that in adults and reductions in myelin which usually can't be detected visually[47]. Myelination occurs during all of childhood and the process continue into adult life.

A study done in 2001 had shown that corpus callosum continues it's growth up to adult life, thus they provided us with in vivo proof that maturation of white matter continues to an age well after somatic growth is completed[47]. Currently, many quantitative imaging methods have contributed by giving an improved perceptive on the myelination process {De Bellis et al.(2001); Giedd et al.(2010); Gur et al. (1999); Iwasaki et al.(1997); Paus et al.(2001); Pfefferbaum et al.(1994); Sowell et al.(2008); Thompson et al., (2000)} [47, 55, 56, 57, 58, 59, 60,61] and the few have told about how white matter myelination in particular neuronal systemare functionally significant{Golestani et al.(2007);Penhune et al(1996); Paus et al.(2001); Thompson et al.(2008)) [62, 63, 47, 61]. For example, recently they had found that there good correlation between the frequency of asymmetry in white matter in regions which are related to the language and also proved increased frequency of left hemisphere dominance for language in right handed children [46]. In this context, children with developmental delay who had shown no evidence of structural brain alterations on assessment after the first myelination stages might present with an overall decrease in myelinated white matter that can be detected by quantitative means.

A Systematic review of MRI findings in a child with DD conducted by Murias et al [64] using 29 studies in 2017 , concluded that different studies had wide variation in definitions of various abnormalities as well as report drastically different rates of abnormalities. They had said that, according to current available evidences, firm recommendations cannot be made regarding the use of neuro-imaging in ID or GDD. MRI is suggested only for children in whom a diagnosis cannot be inspite of a thorough clinical evaluation.

For a higher yield in information, especially in children with structurally normal brain improvement in MR Imaging technologies such as MR Spectroscopy ,Functional MRI, Tractography and Diffusion Tensor Imaging are required.

A study done by Department of Radiology in Cornell University in New York in 2002 [65] on assessment of DD in pediatric children with proton MRS analyzed developmental delay among children with age more than 2 years in which abnormality in the Cho/Cr and NAA/Cr ratios were depicted by proton MRS. The study concluded that Proton MRS must be done as an element of neuro-imaging evaluation in children with developmental delay.

We can study DD children with diffusion tensor imaging (DTI) [66] which is an advanced MRI technique. Verma et al ,in Oct. 2015 had analysed the diagnostic value of metrics derived from diffusion tensor imaging as a way to quantitate cerebral changes in developmental delay on 50 cases and concluded that in children with DD, who have a normal findings on MRI, myelination abnormality can be detected by DTI.

In view of the foregoing, our study was done to assess developmental delay in children in Karnataka using routine and new MRI sequences, which will help clinicians estimate a child's ultimate development potential, guide treatment requirements and allaying parental anxiety.

CORPUS CALLOSUM

Corpus callosum can have many developmental malformations, ranging from agenesis to hypoplasia involving only the splenium. Embryonic development proceeds from anterior part of corpus callosum to the posterior direction leading to a higher frequency of posterior callosal defects if injury occurs during development of corpus callosum. Corpus callosal dysgenesis usually occurs as a result of an injury during the formation of its precursors [67]. However, a direct insult more likely leads to a complete but atrophic corpus callosum [68]. A new classification of callosal abnormalitis was proposed by Jinkins et al.[69] in 1989.Isolated agenesis as well dysgenesism tend to be asymptomatic; and symptoms if present are due to associated anomalies.

SOTO-ARES et al. demonstrated corpus callosum abnormalities (hypoplastic or vertical splenium or short corpus callosum) in about 46% patients with mental retardation in 2003[70]. ZEEGERS et al. had detected alterations in the shape or size of the CC in 9% [71]. Ab-normal morphologies of the CC had also been assessed in a child with mental retardation [72]. Thinning in CC could be due to fewer axons traversing through the corpus callosum or reduction in myelination . However, the volume of fibres in corpus callosum could not explain the "drooping" appearance of the splenium. There is a possibility of abnormal orientation of fibres causing abnormal splenium morphology. FILIPPI et al. studied children with development

delay and using diffusion tensor imaging in 2003 demonstrated decrease in anisotropy and increase in the diffusion constant of white matter, together with the CC, in these children[73]. This decrease in anisotropy may be due to stoppage in myelin maturation to develop normally or due to abnormality in axonal growth. Quantitative evaluation of white matter volume and assessment of the direction of white matter tracts is required through further diffusion tensor imaging based studies in these children.

PERIVENTRICULAR LEUCOMALACIA(PVL)

In a study done by takashilmamura et al in 2013 on nerodevelopmental outcomes in children with DD [74], it was concluded that most grade 2 and 3 PVL was associated with serious neuro-developmental delay, 56% children having grade 1 PVL showed normal psychomotor and rest abnormal development.

Periventricular leukomalacia (PVL) is principal form of underlying brain injury resulting in neurological morbidity. PVL is also the most frequent cause of cerebral palsy (CP) in infants having history of developmental delay. [75]

In the US, 10% of the 55,000(approx.) live very low birth weight newborns born each year develop cerebral palsy. [76]

ROLE OF MR SPECTROSCOPY IN DEVELOPMENTAL DELAY

MR spectroscopy (MRS) measures metabolites in the brain non invasively and thus provides information about structure, maturation and disorders. Some examples of these metabolites whose change in levels is measured spectrally are choline (Cho), lactate , N-acetylaspartate (NAA) and creatine (Cr). Various investigators [77-81] had used MRS for evaluating cerebral metabolism changes during normal white matter myelination and brain maturation . MRS has also been proven to be useful for

assessing developmental delay; metabolic , neurodegenerative, inflammatory, hypoxic–ischemic brain injury, and neuropsychiatric disorders; phakomatosis; and epilepsy [82 -87] .

MRS could be used for detecting differences in brain metabolism of children with idiopathic developmental delay with normal MRI , by explaining the cause of the delay, and help in prognosticating long-term functional outcome by being part of the neuroradiologic assessment of these children.

In a study done by Kosuku et al [88] in 2010 MR spectroscopy was used to determine whether the brain metabolism of children having developmental delay of unknown cause differs from that of children without developmental delay. There was variation in the metabolite distribution in the various regions of the brain but not much considerable difference was found between the brain metabolite ratios in two groups.

Nikhil et al [89] in 2020 compared MRS with MRI in children with DD. They found that MRS added to the diagnostic utility of MRI and recommended MRS to be included as possible diagnostic modality alongside MRI in these subgroup of patients. 64.3% of the cases with normal MRI brain had some or the other abnormality on MRS, NAA/Cr and lipid/lactate being the most frequent abnormal metabolites seen. Furthermore, 10.4% of the children had a MRS blueprint which was suggestive of degenerative /metabolic etiology. The yield of MRS would be increased when MRS pattern is combined with clinical findings for evaluation.

Filippiet al [90] assessed children with developmetal delay with MR Spectroscopy. There was not much statistically considerable difference in NAA/Cr or

Cho/Cr ratio in pediatric children <=2years between children with delay and controls. Children >=2 years of age , showed decrease in the NAA/Cr ratio in the parieto-occipital sub-cortical white matter (WM) and frontal region with P value of<.001 and <.017 respectively . They also showed elevations in Cho/Cr ratio in parieto-occipital sub-cortical WM and frontal region with P value of<.24and <.002 respectively in development delay group compared with controls. Hence, there is a role of proton MRS in imaging evaluation of children with DD. More studies would be needed in the future to determine if proton MR spectroscopy could be used for diagnosis and assessing the long-term functional outcome.

Similar findings were seen in a study by Chellathurai et al [91] on 424 children in 2018, in which they showed MR spectroscopy was abnormal in 73 of the children showing normal MRI.

Verbruggen et al [92] had conducted a cohort study on 325 patients with DD in 2009. They found 9% cases of development delay showed abnormal MRS findings and2.7% showed abnormal neurologic findings. It helped in the diagnosis in 1 of the cases. Majority children showed minor abnormalities, whereas MRI or/and MRS contributed to diagnosing the etiology in only 9% of cases (all were scanned due of presence of neurological signs). Out of these 10 patients, MRS was problem-solving in one of the patients and was of supplementary value to MRI findings in 3 of the cases. Hence it was Concluded that: MRI1/1HMRS combination may be etiologically diagnostic in patients with neurological signs of development delay, whereas their function was less when these signs are absent

In a study done from july 2001 to september 2003 by Augustine et al [93] 36 infants with birth weight less than 1510 and gestational age less than 32 weeks were

analysed with MR spectroscopy at postmenstrual age of 35 -43 weeks. There was no significant correlation between metabolic ratios and the developmental outcome in these children. Nevertheless, significant correlation was noted between NAA)/Ch and postmenstrual age in the thalamus and the basal ganglia.

Filippi et al,[90] Fayed et al,[94] and Hashimoto et al,[95] had similar conclusion showing statistically remarkable difference in the different metabolic ratios in paediatric patients with developmental delay v/s control pateints, supporting role of MRS as a supplementary modality in diagnosing children with developmental delay.

Fayed et al [94] concluded in his study done in 2006 that MR Spectroscopy could provide crucial information in children with neuro-developmental disorders, low NAA/Cr ratio could be seen as a good marker of DD and MRS could be used to identify changes in the WM such as delayed myelination in children with DD. They had done this study on 12 children meeting the criterion of DD between 3 to 12 years and 11 healthy children control children on whom standard MRI and MRS was done. There was noteworthy decrease in the level of NAA/Cr, NAA/Ch , and NAA/mI ratios in children with idiopathic intellectual disability in relation to controls with a P value < .016, < .026 and< .023 respectively. There was not much significant differences in rest of the metabolic ratios.

Changes in developmental brain were analysed with proton magnetic resonance spectroscopy by Hashimoto in 1995 [95] .In this study, they had done volume-selective proton magnetic resonance spectroscopy (1H-MRS) using a 1.5 Tesla magnet on 47 healthy children and in 6 healthy adults. They had seen N-acetylaspartate (NAA),creatine (Cr) and choline (Cho) peaks in the right parietal region in all the cases, with lactate peak in none of the cases. Increase in NAA/Cho ,

NAA/Cr and a decrease in Cho/Cr rations were noted in the right frontal region in 21 cases with advancing age with most speedy change between one to three years of age. Hence , in their study they had concluded that co–relation of developmental changes and regional variation of metabolites on 1H-MRS of the brain need to be studied further for its application.

According to study done by Krijn T [96] in 2009 , MRI is able to detect abnormalities in more than 80% of children with development delay, 1HMRS in 10%. MRI/1HMRS combination helps in diagnosis in 10(9%) which is a small but considerable number.1HMRS could be diagnostic if highly distinctive metabolite patterns are picked up, or else add value to structural MRI in evaluation of children with development delay.

Treatment / Management

A child with developmental delay requires multimodal and multi-speciality management which involves primary care providers , pediatric specialists like pediatric-neurologists,child psychiatrists, behavioral and developmental pediatricians, and other pediatric subspecialists, genetics, psychology, , speech & language, physical therapy, occupation therapy ,and nutritionists, etc.

Treatment strategy requires that the primary care provider, (lead member of the team) creates a therapeutic collaboration with the pediatric department , giving parents required facts about the DD , educating about any developing syndromes, together with the diagnosis, course of the disorder, prognosis, and complication. Moreover, parental counseling/guidance and psychosocial support and are important elements of care. Parental understanding is key to adherence to care plans and acceptance.[8]

Social support services such as regular home visits and transportation service might be essential to finish off evaluation.[15] Sometimes, significant clinical concerns with parents appearing not to comprehend or be in denial about it existence, then follow-up appointment could be helpful with the primary care provider during the DD evaluation.[7] Few other suggestions for early referrals and interventions are as follows:

1. Timely intervention programs
2. Timely childhood education
3. Timely periodic screening, diagnostic, and treatment (EPSDT)
4. To consider referring the child to adolescent psychiatrist or /and behaviour therapists in case of behavioural problems
5. To consider referring children having parent training. This includes providing children with appropriate simulating environment at home, daycare and school. Referral could be made to these community-based services.
6. To consider children for group social skills training in case of social skill difficulty in child
7. To consider referring to ophthalmology in case of visual deterioration
8. To consider referring to audiology in case of auditory deterioration
9. To consider referring for therapy in case of gross of fine motor delay
10. HeadStart
11. To consider referring to a speech and language pathologist in case of speech delay
12. Other community programs and service agencies [9,15,97]

MATERIALS AND METHODS:

7.1 Source of data:

Paediatric patients in the age group of 2 month to 7 years with developmental delay referred to Department of Radio-Diagnosis at the Dr.Prabhakar Kore Hospital & MRC, at KLE University , Belagavi.

7.2 Method of collection of data:

a) **Study design:** Hospital based Cross sectional study

b) **Sample size:**

The minimum sample size formula based on prevalence rate is

$$n = \frac{z_\alpha{}^2 P(1-P)}{d^2}$$

where P is defined as percentage of prevalence and d is the percentage likely difference in the prevalence.

z_α is linked with the level of significance. For 5% level of the significance z_α = 1.96.

Ref:

A study by Ali et al,[44] in Deccan college of medical college of medical sciences, Hydrabad, India in 2015 studied the prevalence of normal and abnormal MRI in pediatric patients presenting with developmental delay, it was found that 68% of the patients had abnormal findings.

With P = 68% and d = 25% of P = 10%, the sample size was 30

(a) Sampling method: Universal sampling

All the eligible subjects were recruited into the study consecutively for a period of one year between 1st January 2020 to 31st December 2020.

(b) The diagnosis of global developmental delay(GDD) was made by paediatric-neurologist, who then referred the patients for brain MRI brain to rule out the structural causes for the DD. Diagnosis of GDD was made if child failed to meet one or more than one normal developmental milestones in terms of speech or language skills, motor skills, social skills and education. All patients will be evaluated clinically and then MRI of the brain will be performed using a 3.0 Tesla MRI scanner.

(c) Study Duration :One year – between 1stJanuary 2020 to 31stDecember 2020

(d) Inclusion criteria:

Paediatric patients in the age group 2 month to 7 years with DD with not a known cause attending Department of paediatrics at KLE Dr Prabhakar Kore Hospital & MRC

(e) Exclusion criteria:

- Children aged more than 7 years
- Postnatal causes of developmental delay like trauma
- Patients with known Genetic Disorders such as Down syndrome, Turners Syndrome
- Children with neurocutaneous syndromes

(f) Ethical considerations:

Study was approved by the institutional human ethics committee. Informed consent from all the study participants and those participants willing to sign the informed consent were included in the study was taken. The risks and benefits involved in the study and voluntary nature of participation were explained to the participants before obtaining consent. Confidentiality of the study participants was maintained.

(g) Data collection tools:

Questionnaire proforma was filled for all study participants containing socio-demographic data, history, clinical examination and MRI scan findings

(h) Method of Statistical data analysis:

Abnormal MRI findings were considered as primary outcome variable. Demographic and clinical history parameters like age, gender etc were considered as secondary variables.

Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency and proportion for categorical variables. Data was also represented using appropriate diagrams like pie diagram, bar diagram and box plots.

Methodology:

Institutional ethical clearance was taken for the study.

Written informed consent from all study participants was taken.

Study was done using 3.0 Tesla MRI machine manufactured by Siemens after making the child sleep/sedated/anesthetized.

Standard scan protocol was followed for all the patients undergoing MRI.

Once the MRI was done, findings were noted and analysed

All the data was collected and was coded, entered in excel sheets, data analysis was done and statistical testes were applied.

EQUIPMENT: 3.0T MRI manufactured by Siemens

MRI SEQUENCES THAT WERE OBTAINED:

1. Axial T1TSE
2. Axial T2TSE
3. Axial T2FLAIR
4. Axial EP2D diffusion
5. Axial T2TIRM
6. Axial PDTSE
7. Axial 3D T2SWI
8. Coronal T1TIR
9. Coronal T2TSE
10. Sagittal T1TSE
11. Point Resolved spectroscopy (PRESS) Sequence

RESULTS

Table 1: Age Distribution Of Study Population With Normal And Abnomal Mri Findings

MRI FINDINGS	NORMAL		ABNORMAL	
AGE(YEARS)	NUMBER	PERCENTAGE	NUMBER	PERCENTAGE
<1 years	2	8.33	19	31.15
1-3 years	16	66.67	18	29.51
3-5years	2	8.33	6	9.84
>5years	4	16.67	18	29.51
Total	24	100	61	100

The study population was distributed into different age groups. The children were further divided into those with abnormal and normal MRI findings. 23.52% (20/85) of the children belonged to <1 years of age, 40.0 % (34/85) of the children belonged to 1 to 3 years of age , 22.85 % (8/85) of the children belonged to 3-5 years of age.

Graph 1: Age Distribuation Of Study Population With Normal And Abnomal Mri Findngs

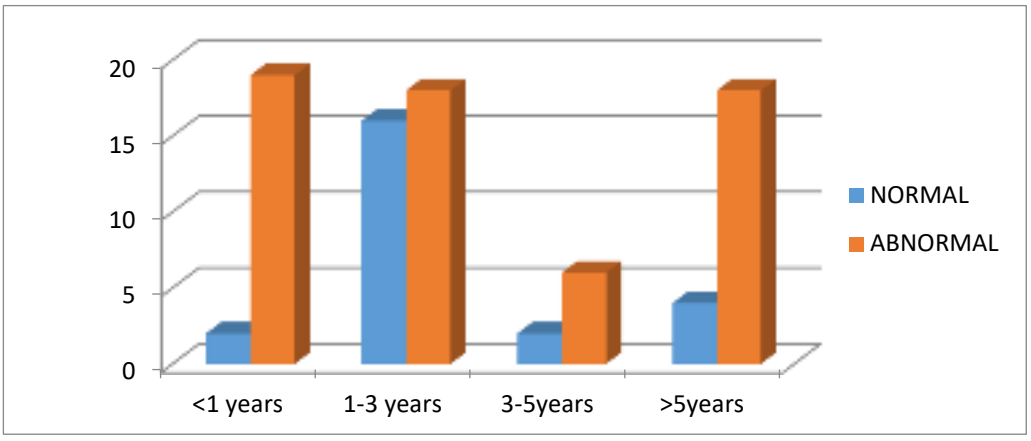


Table 2: Sex Distribuation Of Study Population With Normal And Abnomal Mri Findngs

	NORMAL		ABNORMAL	
GENDER	**NUMBER**	**PERCENTAGE**	**NUMBER**	**PERCENTAGE**
MALE	**9**	**37.5**	**17**	**27.87**
FEMALE	**15**	**62.5**	**44**	**72.13**
TOTAL	**24**	**100.0**	**61**	**100.0**

The study population was distributed into males and females groups , which were further subdivided into abnormal and normal findings. 30.59%(26/85) were males and 69.41 %(59/85) children were females which was considered due to chance.

Graph 2: Sex Distribuation Of Study Population With Normal And Abnomal Mri Findngs

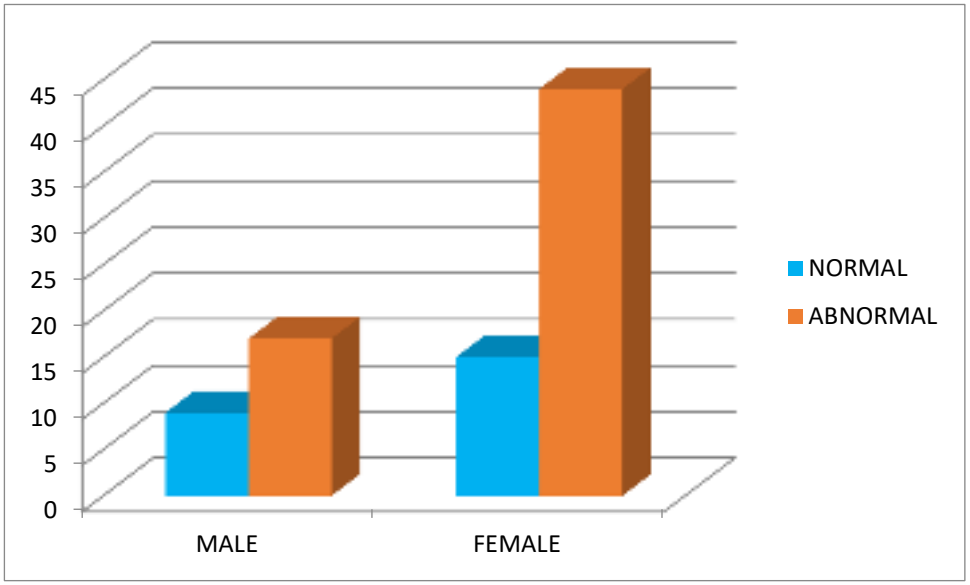


Table3: Distibution According To Etiology

ETIOLOGY	NUMBER	PERCENTAGE
HYPOXIC ISCHEMIC INSULT	16	18.82
CONGENITAL/DEVELOPMENTAL	22	25.88
METABOLIC	16	18.82
POST INFECTIOUS	3	3.52
NEOPLASTIC ETIOLOGY	2	2.35
NON SPECIFIC	8	9.41

The study population were distributed into aetiological categories; in which congenital/developmental anamolies ranked highest in our study(25.88%), Traumatic/ Neurovascular Diseases (Hypoxic Ischemic Brain Injury)(18.82) and metabolic cause(18.82) ranked the second highest , followed by unknown cause (9.41%) , infectious etiology (3.52)and neoplastic etiology(2.35%).

Graph 3: Distibution According To Etiology

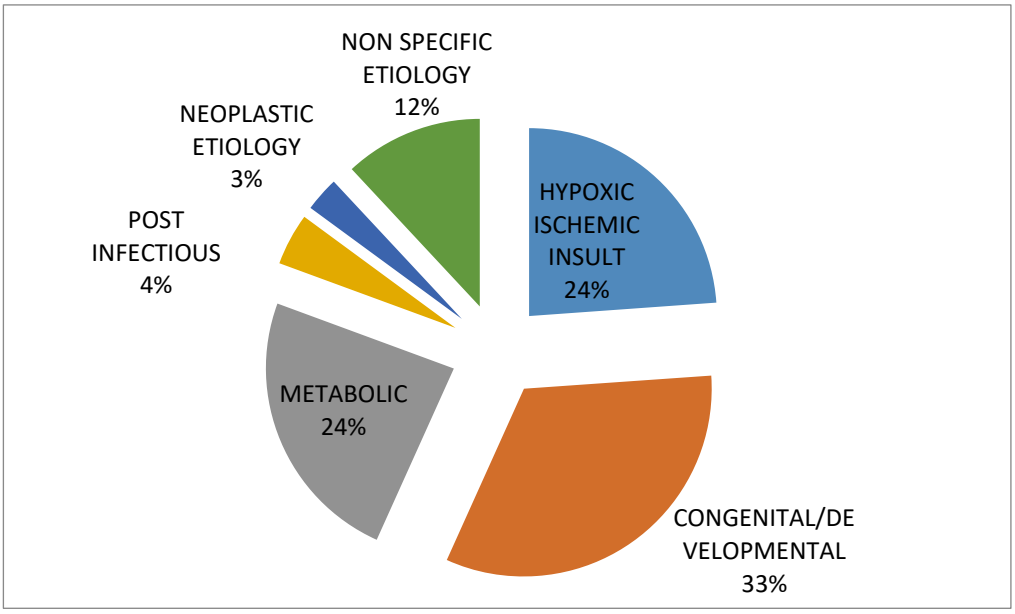
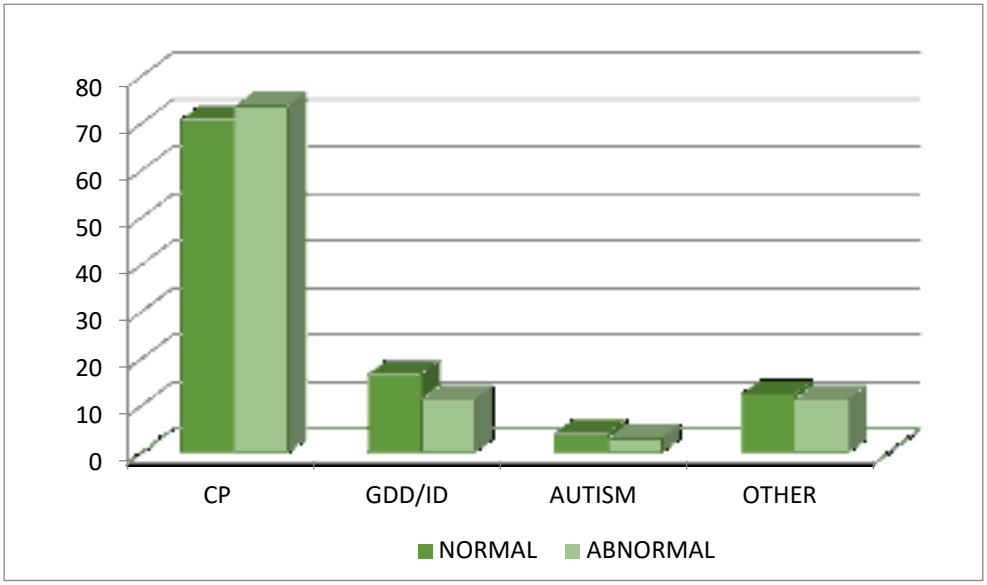


Table 4: Distribution According To Clinical Diagnosis

CLINICAL DIAGNOSIS	NORMAL		ABNORMAL	
	NUMBER	PERCENTAGE	NUMBER	PERCENTAGE
CERBRAL PALSY	17	70.83	45	73.77
GDD/ID	4	16.67	7	11.48
AUTISM	1	4.17	2	3.28
OTHER	3	12.5	7	11.48

Graph 4: Distribution According To Clinical Diagnosis

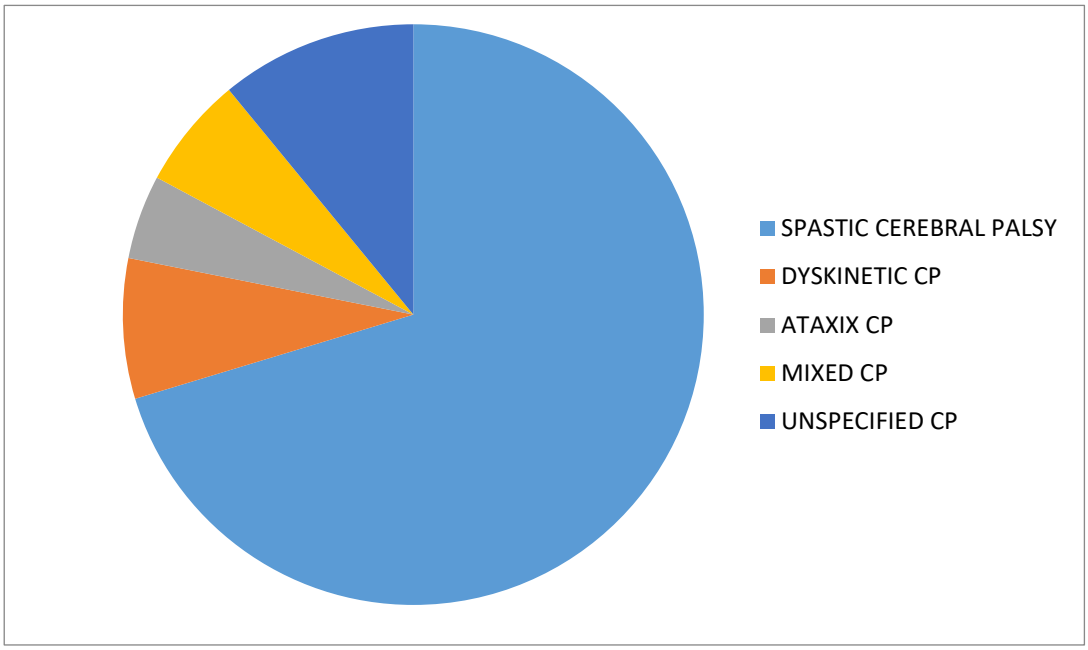


72.94 % (62/85) of the children were clinically diagnosed to have cerebral palsy, out of which 72 .58 % (45/62) had abdnormal MRI brain findings . 12.94 % (11/85) of the study population were diagnosed to have global developmental delay/ intellectual disability pattern of clinical presentation out of whome 63.63% (7/11) had abnormal MRI brain. Only 3.52 % (3/85) of the population had autism like clinical presentation. Rest of the study population (11.76 %) had other clinical diagnosis.

Table 5: Distribution According To The Type Of Cerebral Palsy

TYPE OF CEREBRAL PALSY	NUMBER	PERCENTAGE
SPASTIC CEREBRAL PALSY	45	72.58
DYSKINETIC CP	5	8.06
ATAXIX CP	3	4.83
MIXED CP	4	6.45
UNSPECIFIED CP	7	11.29

Graph 5: Distribution According To The Type Of Cerebral Palsy



Out of the children 62 children diagnosed to have cerebral palsy , 72.58 % (45/62) children had spastic cerebral palsy, 8.06%(5/62) had dyskinetic cerebral palsy, 4.83% (3/62) had ataxic cerebral palsy, 6.45% (4/62) had mixed cerebral palsy and 11.29% had unspecified cerebral palsy.

Table 6:Distribution According To Clinical Presentation Of Study Group

CLINICAL PRESENTATION	NORMAL		ABNORMAL	
	NUMBER	PERCENTAGE	NUMBER	PERCENTAGE
ONLY DEVELOPMENTAL DELAY	14	58.33	27	44.26
DEVELOPMENTAL DELAY + SEIZURES	1	4.17	18	29.51
DEVELOPMENTAL DELAY + OTHER HISTORY	9	37.50	16	26.23

48.23% (41/85) of the population had presented only with developmental delay, 22.35%(19/85) had presented with developmental delay plus seizures as clinical presentation , 29.41% (25/85) of the population had presented with developmental delay with other clinical history.

Graph 6: Distribution According To Clinical Presentation Of Study Group

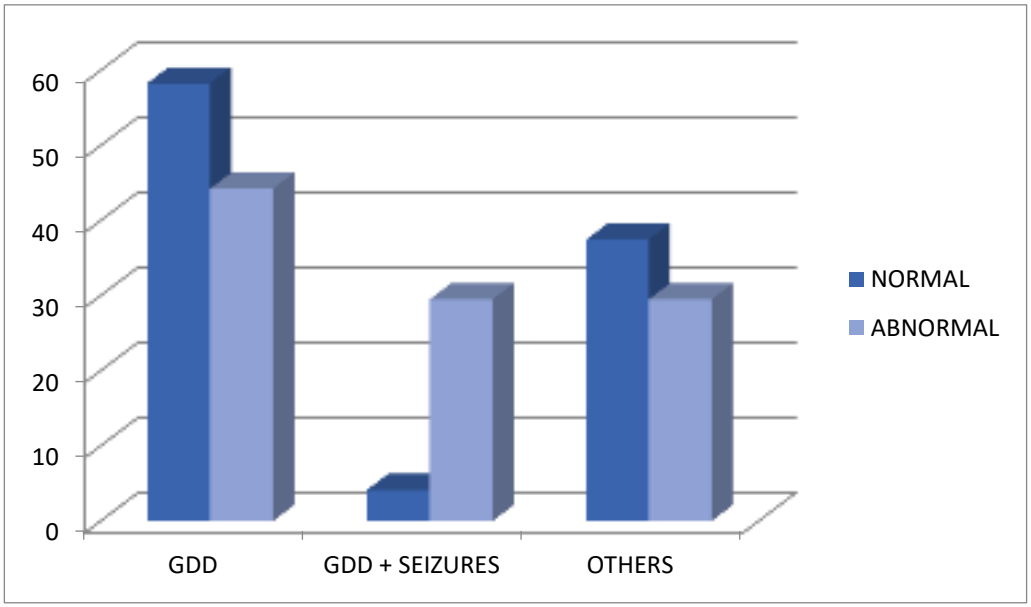
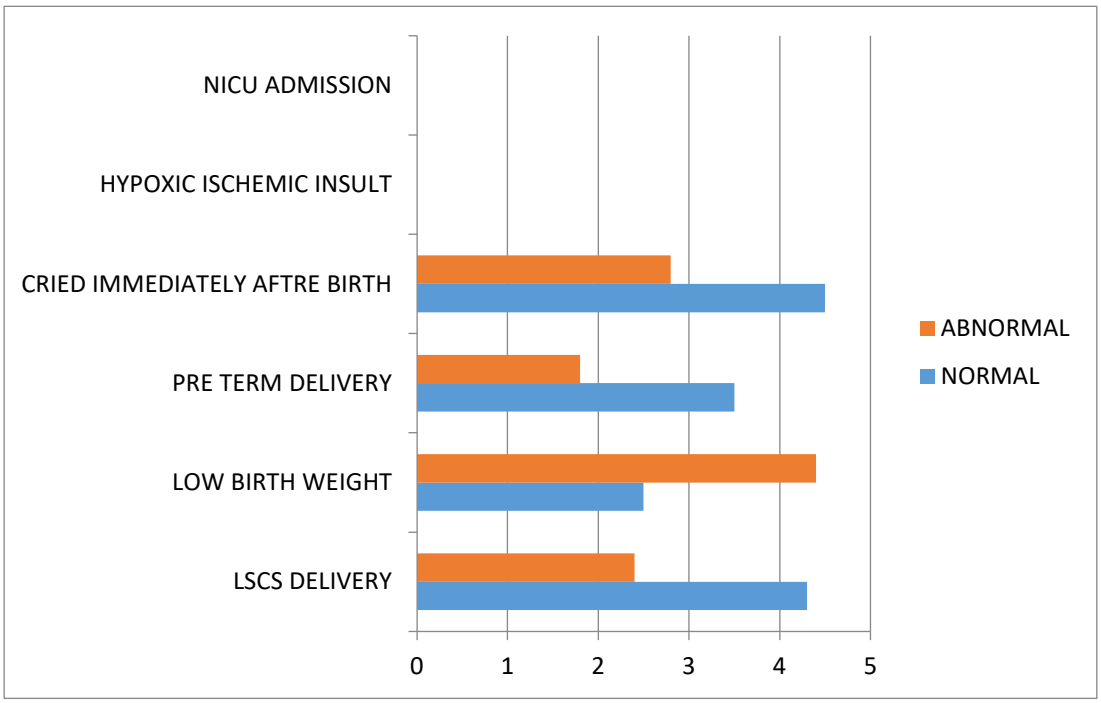


Table 7 :Distribution According To Birth History

	NORMAL		ABNORMAL	
BIRTH HISTORY	**NUMBER**	**PERCENTAGE**	**NUMBER**	**PERCENTAGE**
LSCS	**8**	**9.41**	**18**	**21.17**
LOW BIRTH WEIGHT	**3**	**3.52**	**23**	**27.05**
PRE-TERM	**4**	**4.70**	**16**	**18.82**
CIAB	**9**	**10.58**	**31**	**36.47**
HYPOXIC INSULT	**17**	**2.00**	**41**	**48.23**
NICU ADMISSION	**2**	**2.35**	**18**	**2.11**

Graph 7 :Distribution According To Birth History



30.59 % (26/85) of the study population had history of cesarean section delivery, out of which 6.92% (18/26)had abnormal findings. 30.59% (26/85) children had history of low birth weight out of which 8.85% (23/26) had abnormal findings. 23.52 (20/85) children had history of pre term delivery. Out of which 80.00%(16/20) had abnormal findings. 47.05 %(40/85) of the children had cried immediately after birth in which 36.47 % (31/85) had abnormal findings. 68.23 %(58/65) children had history of hypoxic insult, majority 48.23 % (41/85) had abnormal findings, and 23.52(20/85) children had history of NICU admission out of which 90.00% (18/20) had abnormal findings.

Table 8 : Distribution Acording To History Of Consanguineous Marriage

	NORMAL		ABNORMAL	
	NUMBER	PERCENTAGE	NUMBER	PERCENTAGE
CM	6	25.00	18	75.0

The study population distributed according history of consanguineous marriage and MRI findings. 24 /85 (28.23%) had history of marriage within the family. Out of these 6/24(25%) had normal MRi brain findings and 18 / 24 (75%) had abnormal mri brain findings

Graph 8 : Distribution Acording To History Of Consanguineous Marriage

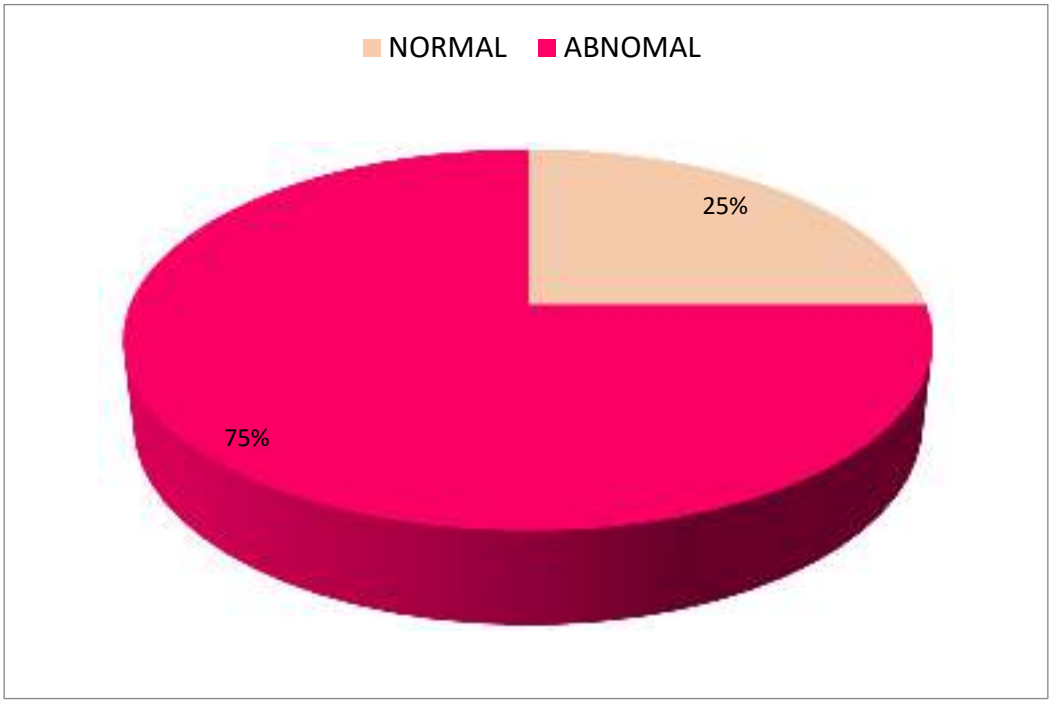


Table9 :Distriution Of Children With History Of Consanginious Marriage According To Past History

PAST HISTORY	NUMBER	PERCENTAGE
Hypoxic ischemic injury	**3**	**16.66**
Developmental etiology	**8**	**44.44**
Metabolic etiology	**3**	**16.66**
Post infectious	**2**	**11.11**
Neoplastic etiology	**0**	**0**
Non specific	**2**	**11.11**

Out of 18 children with history of consanguineous marriage , majority of patients had had congenital/ developmental abnormality.8/18(44.44%). 3 out of 18 had history of hypoxic ischemic insult. 3 out of 18 also had metabolic etiology. 2 out of 18 had infectious etiologic.

Graph 9:Distriution Of Children With History Of Consanginious Marriage According To Past History

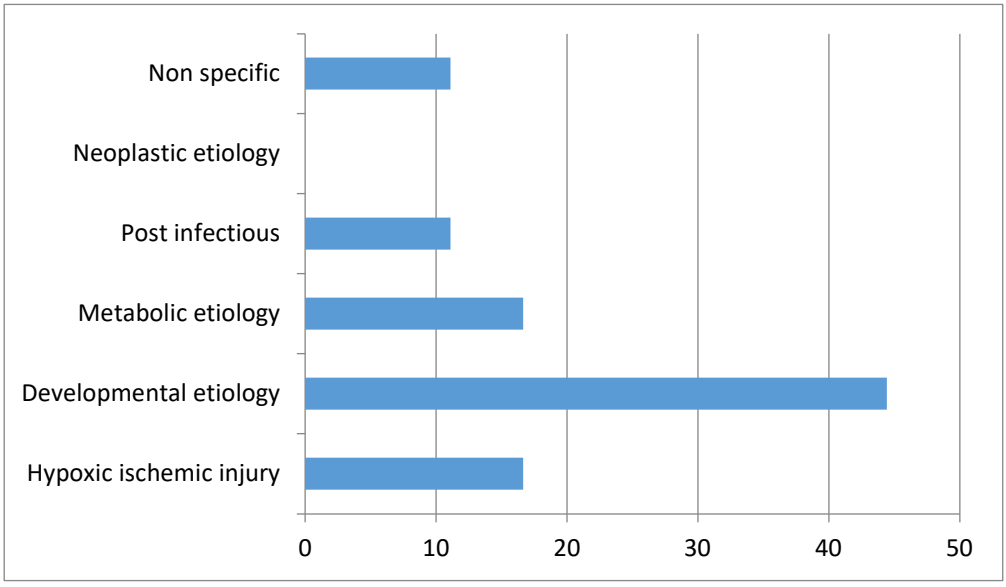


Table 10: Distribution According To MRI Findings In Relation To Head Size

HEAD SIZE	NORMAL		ABNORMAL	
	NUMBER	PERCENTAGE	NUMBER	PERCENTAGE
NORMAL HEAD SIZE	20	83.33	52	85.25
MACROCEPHALY	2	8.33	3	4.92
MICROCEPHALY	2	8.33	6	9.84

The study population was distributed based on relation to the head size, 84.70 % (72/85) of the children had normal head size. Only 5.88% (5/85) of the children had macrocephaly and only 9.41 % (8/85) had microcephaly. 75.0% of the children with microcephaly and 60.0 % of the children with macrocephaly had abnormal brain findings.

Graph 10: Distribution According To MRI Findings In Relation To Head Size

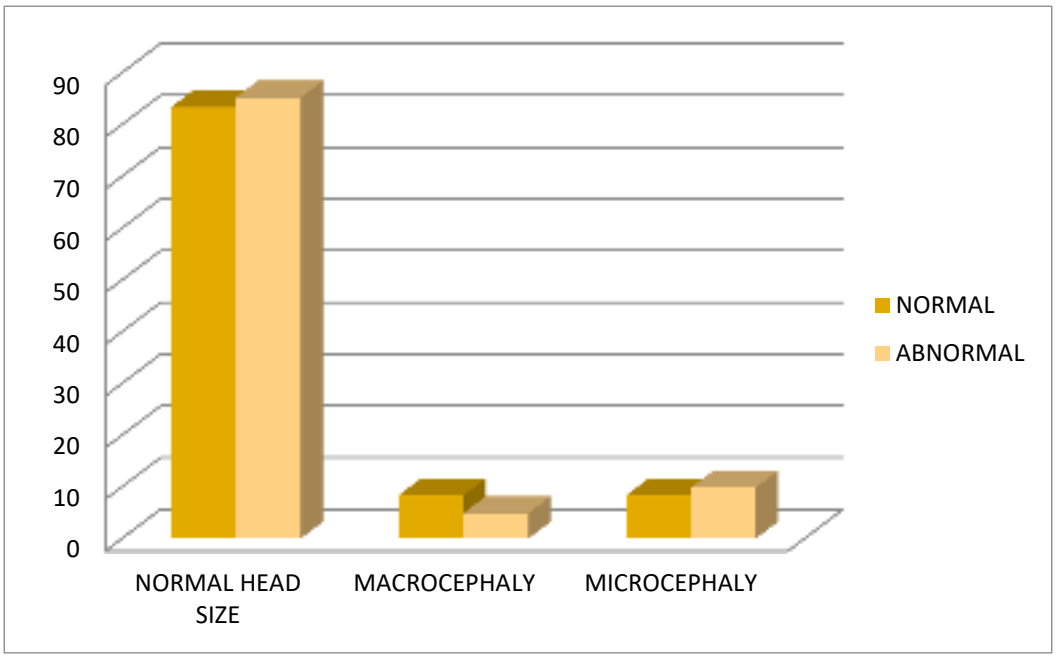
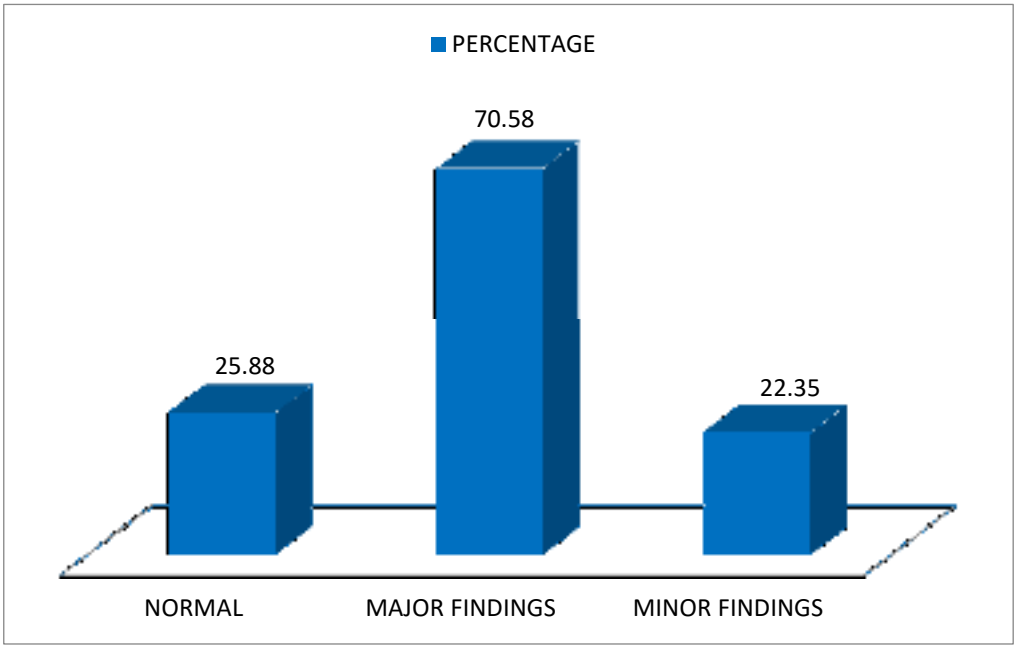


Table 11: Distribution According To MRI Findings

MRI FINDINGS	NUMBER	PERCENTAGE
NORMAL	22	25.88
MAJOR FINDINGS	60	70.58
MINOR FINDINGS	19	22.35

Graph 11: Distribution According To MRI Findings



Of the 79 patients with abnormal MRI findings, cortical grey matter abnormalities were seen in 18/85 (21.18%), Abnormal ventricles were seen in 34/85 (40.0%); abnormal corpus callosum was identified in 21/85 (24.1%) and white matter excluding corpus callosum in 35/85 (41.18). Other MR findings included abnormalities in the medial temporal lobe (9/85, 10.59%), basal ganglia(8/85, 9.41%), cerebellum 13/85,15.29%), and brainstem (5/85, 5.88%). Delayed myelination was seen in 1 out 85 patients (1.17%).

Table 12 : Distribution According To Type Of Major MRI Abnormalities

MAJOR ABNORMALITY	NUMBER	PERCENTAGE
CORTICAL GREY MATTER	18	21.18
WHITE MATTER	35	41.18
MEDIAL TEMPORAL LOBE	9	10.59
VENTRICLES	34	40.0
BASAL GANGLIA	8	9.41
CORPUS CALLOSUM	21	24.71
BRAINSTEM	5	5.88
CEREBELLUM	13	15.29
DELAYED MYELINATION	1	1.17

Graph 12 : Distribution According To Type Of Major MRI Abnormalities

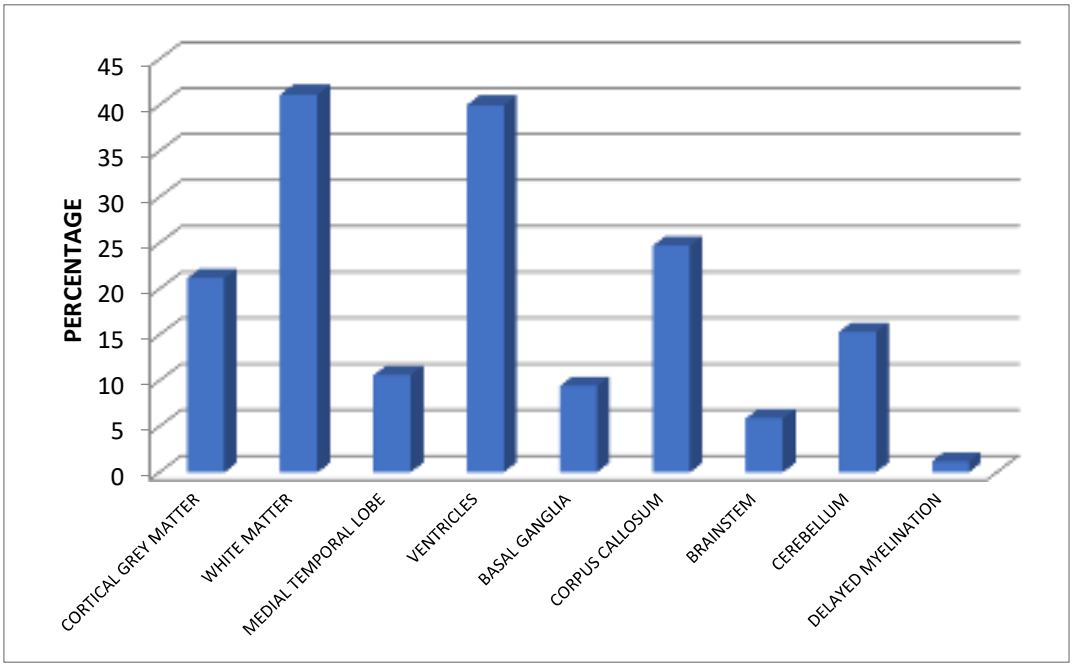


Table 13: Distribution Of Minor MRI Abnormalities

	NUMBER	PERCENTAGE
MEGA CISTERNA MAGNA	38	44.70
DILATED VR	11	12.94
CYSTS	2	2.35
CAVUM SEPTUM PELLUCIDUM/VERGAE/INTERPOSITI	22	25.88
ENLARGED SUB ARACHNOID SPACE	36	42.35

19 out of 85 patients(22.35 %) had minor abnormities such as dilated virchow robin spaces (12.94%), mega cistern magna(44.70%), arachnoid cyst, cavum septum pelucidum/vergae /interpositum (25.88%) and enlarged subarachnoid spaces(42.35%).

Graph 13: Distribution Of Minor MRI Abnormalities

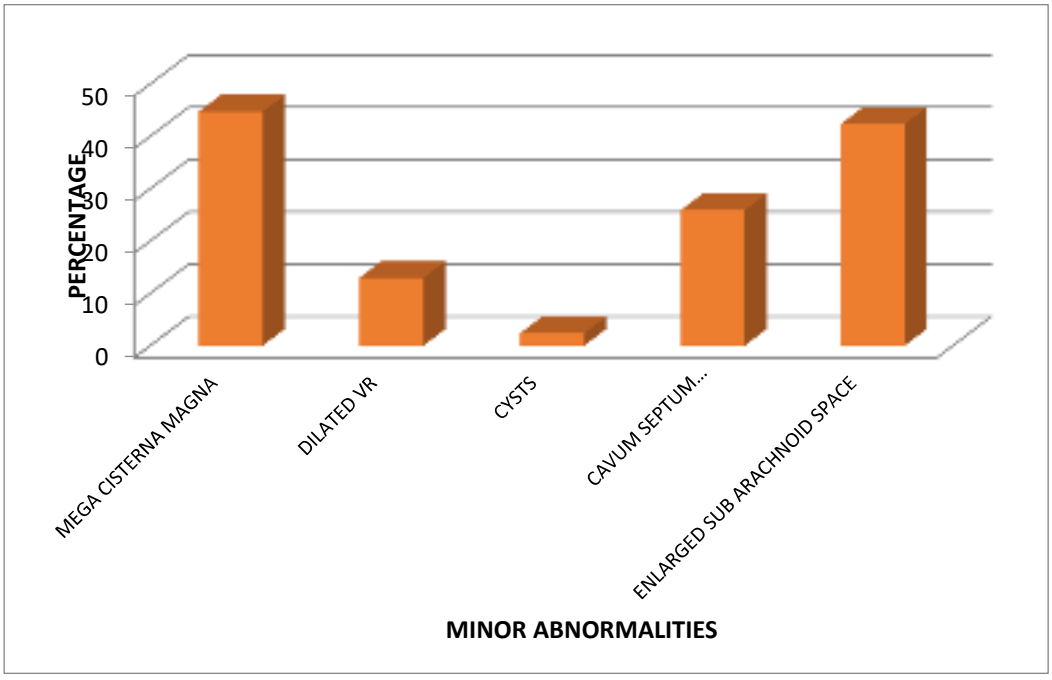
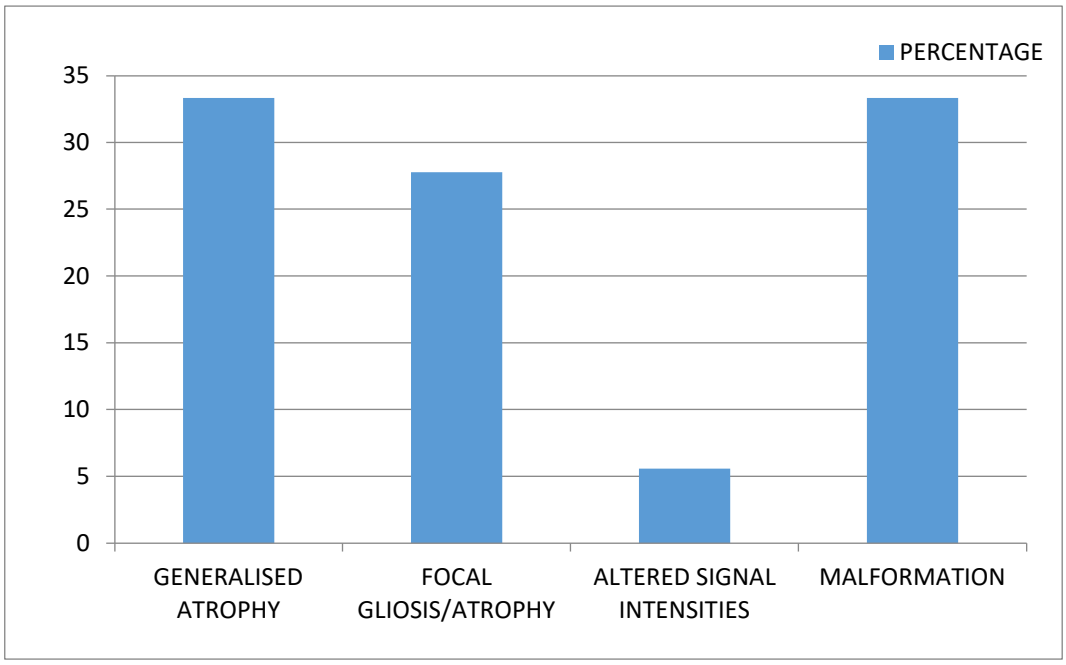


Table14 : Distribution According To Abnormalities In Grey Matter

CATEGORIES	NUMBER	PERCENTAGE
GENERALISED ATROPHY	6	33.33
FOCAL GLIOSIS/ATROPHY	5	27.78
ALTERED SIGNAL INTENSITIES	1	5.56
MALFORMATION	6	33.33

Graph 14 : Distribution According To Abnormalities In Grey Matter



Amongst the cases with abnormalities in the grey matter (21.18%) , 33.33%(6/18) showed generalised atrophy , 27.78%(5/18) showed focal area of gliosis or atrophy, 33.33 % (6/18) showed cortical malformations and 5.56% (1/18) showed altered signal intensities.

Table 15 : Distribution According To Abnormalities Of White Matter

ABNORMALITY	NUMBER	PERCENTAGE
FOCAL GLIOSIS	8	22.86
PAUCITY OF WM	6	17.14
FOCAL ALTERED SI	7	20.0
DIFFUSE ALTERED SI	8	22.86
NEOPLASM	1	2.85
MALFORMATION	3	8.57
DELAYED MYELINATION	1	2.85

Amongst the children having abnormalities in the white matter , 22.86% of the patients had focal gliosis , 17.14% of the patients had paucity of the white matter, 22.86% of the cases had focal altered signal intensity, 22.86% of the cases show diffuse altered signal intensity , 2.85% of the case showed neoplasm involving the white matter, and only 2.85% showed delayed myelination.

Graph 15: Distribution According To Abnormalities of White Matter

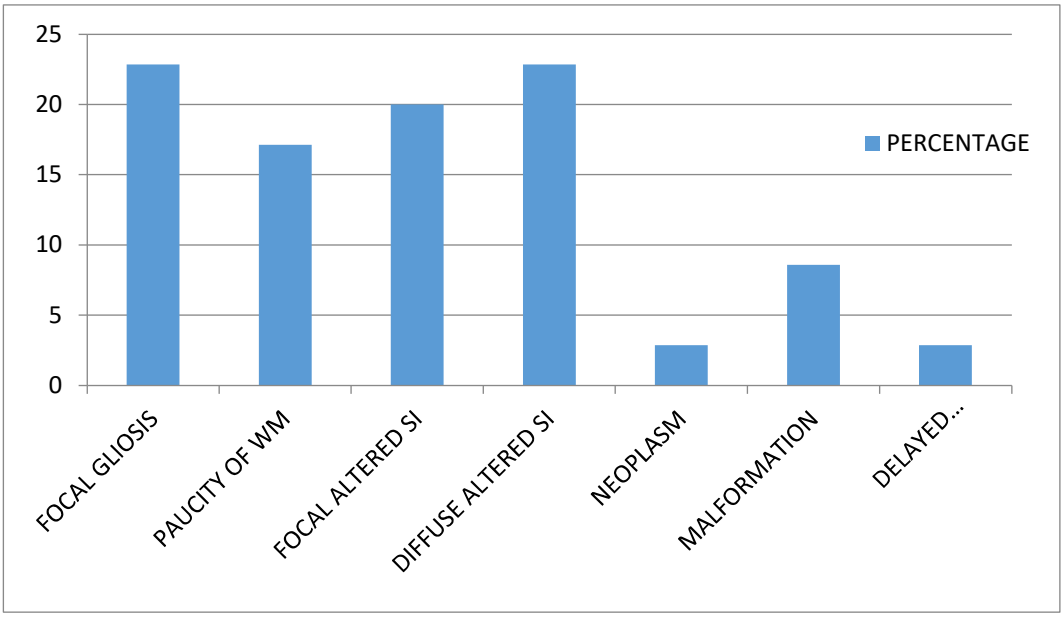


Table 16 : Distribution Of Cerebellar Abnormalities

ABNORMALITY	NUMBER	PERCENTAGE
VERMIAN HYPOPLASIA	5	36.46
BILATERAL CEREBELLAR HYPOPLASIA	2	15.38
UNILATERAL HYPOPLASIA	1	7.69
CEREBELLAR + VERMIAN HYPOPLASIA	1	7.69
DYSPLASIA	2	15.38
GLIOSIS	1	7.69
MACROCEREBELLUM	1	7.69

Amongst the children having cerebellar abnormalities , the most common abnormality was vermian hypoplasia with 36.46%(5/13) of the total cerebellar cases, 15.38%(2/13) had bilateral mild cereblar hypoplasia, 15.38%(2/13) had cerebellar dysplasia, 7.69% (1/13) had unilateral hypoplasia, 7.69% (1/13) had both cerebellar and vvermian hypoplasia, 7.69% (1/13) had gliosis in cerebellum and 7.69% (1/13) had macrocerebellum.

Graph 16 : Distribution Of Cerebellar Abnormalities

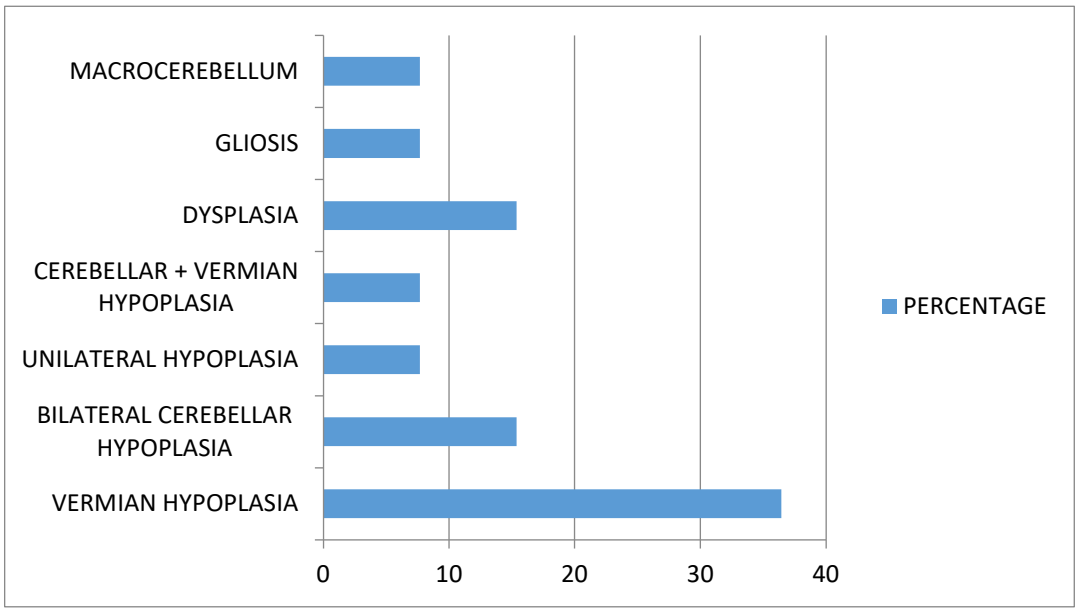
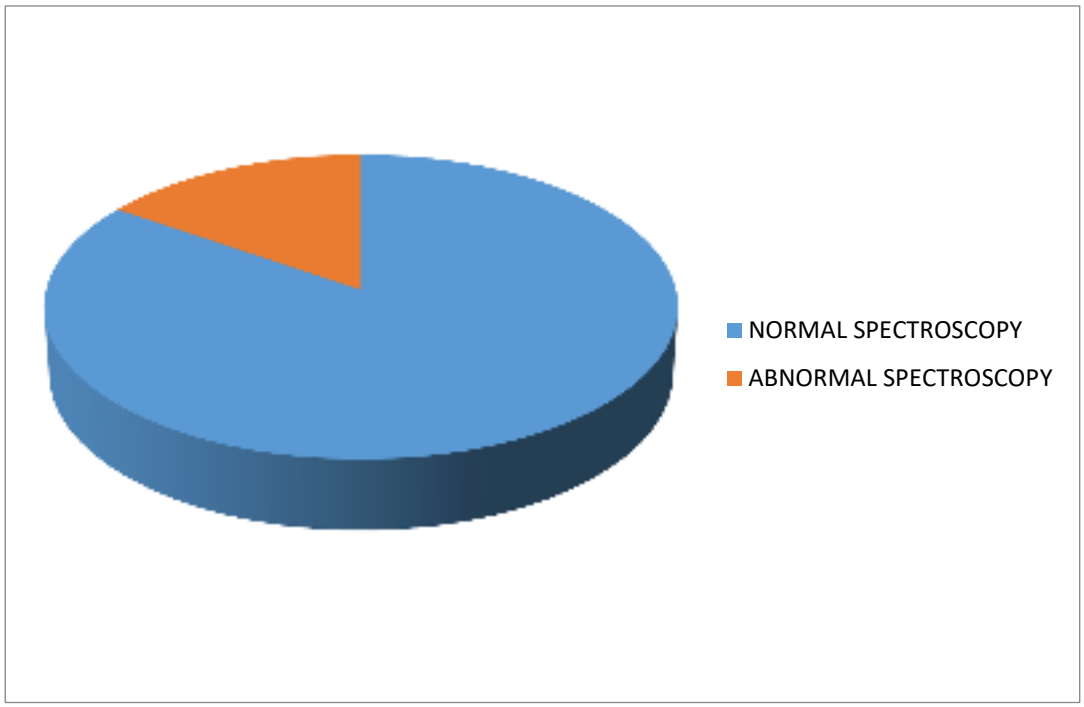


Table 17: Percentage Of Patients With Abnormal Or Normal Spectroscopy With Metabolic Disorders

	NUMBER	PERCENTAGE
NORMAL SPECTROSCOPY	11	84.61
ABNORMAL SPECTROSCOPY	2	15.38

Graph 17: Percentage Of Patients With Abnormal Or Normal Spectroscopy With Metabolic Disorders



Amongst the cases with cerebellar abnormalities, only 15.38 %(2/13) of the cases had abnormal spectroscopy findings.

Table 18: Distribution Of Patients With Cerebellar Abnormalities According To Etiology

ETIOLOGY	NORMAL	PERCENTAGE
HYPOXIC /TRAUMATIC INJURY	2	15.38
DEVELOPMENTAL ETIOLOGY	3	23.07
METABOLIC ETIOLOGY	5	36.54
NON SPECIFIC	3	23.07

Amongst the children with cerebellar pathologies, majority of the cases [36.46%(5/13)] had metabolic etiology, 15.38%(2/13) had hypoxic etiology. Whereas of the 27.07 % (3/13) cases had developmental etiology, rest were non specific.

Graph 18 :Distribution Of Patients With Cerebellar Abnormalities According To Etiology.

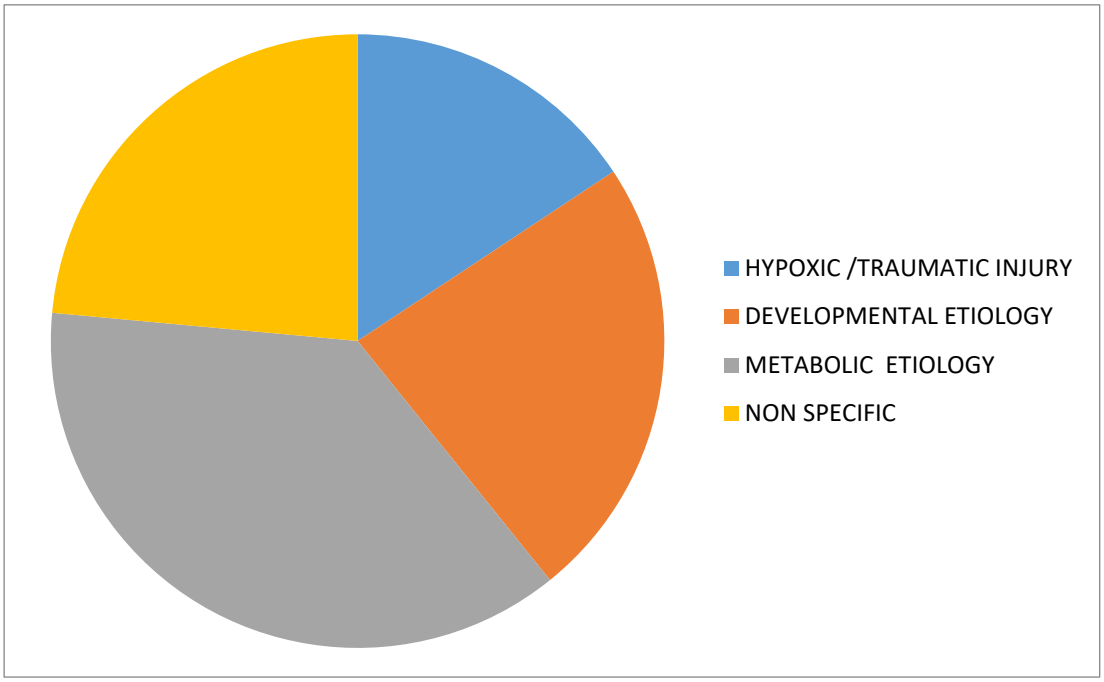


Table 19: Distribution According To Corpus Callosum MRI Findings

	NUMBER	PERCENTAGE
MILD DIFFUSE THIINING	7	8.33
SEVERE DIFFUSE THIINING	3	3.53
ANTERIOR THIINING	1	1.18
POSTERIOR THIINING	4	4.71
THINNED BODY	4	4.71
AGENESIS	3	3.53
SIGNAL ABNORMALITIES	1	1.18
ABNORMAL ORIENTATION OF SPLENIUM OF CC	1	1.18
NORMAL	62	72.94

Amongst the 85 children, 22 cases (45.45%) showed abnormalities in the corpus callosum which were distributed into the types of abnormalities, 8.33% of the study populationshowed mild diffuse thinning, 3.53% showed severe diffuse thinning, 1.18 % showed anterior thinning, 4.71 % showed posterior thinning, 4.71 % showed thinned out body, 3.53% showed complete agenesis,1.18% showed signal abnormalities and 1.18%(1 case) showed abnormal orientation of splenium of corpus callosum.

Graph 19: Distribution According To Corpus Callosum MRI Findings

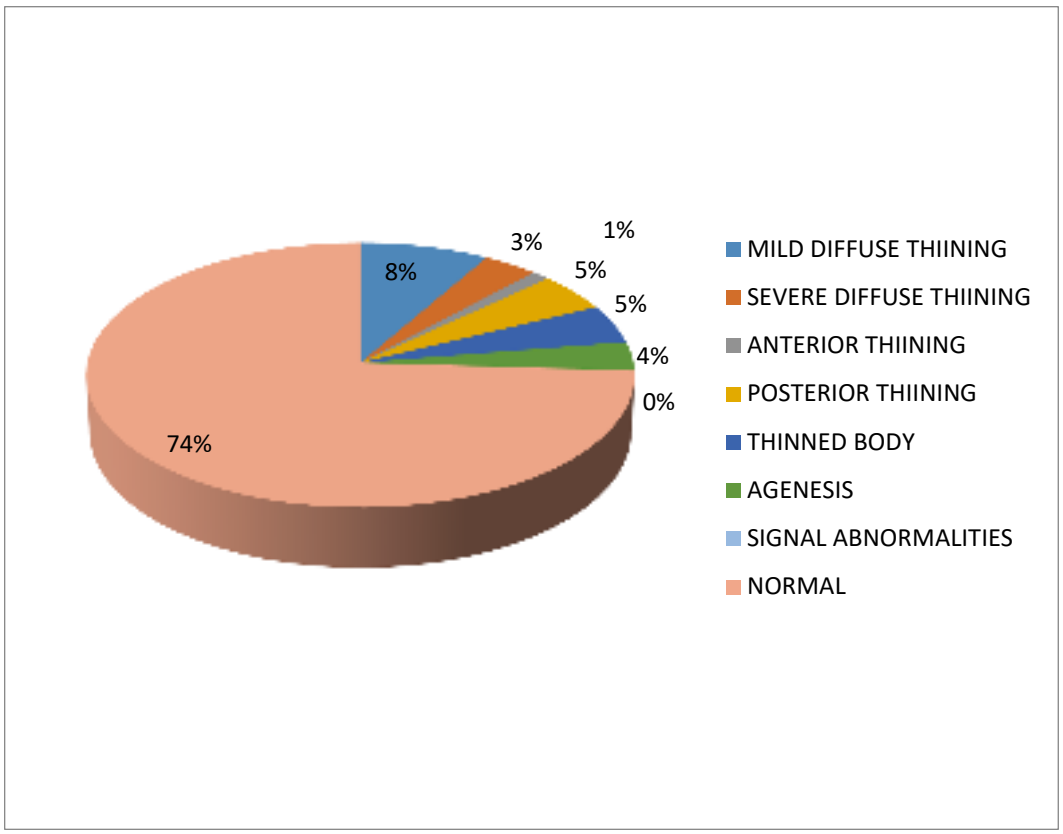


Table 20: Distribution According To Ventricular Abnormalities

	NUMBER	PERECENTAGE
SYMMETRICALLY DILATED	13	15.29
ASSYMETRICALLY DILATED	10	11.76
EX VACUO DILATATION	6	7.06
COLPOCEPHALY	3	3.53
OTHERS	4	4.71
NORMAL	51	60.0

Amongst the 25 cases showing abnormalities in the ventricles , 15.29% showed symmetrical dilatation of ventricles, 11.76% showed asymmetrical dilatation of the ventricles, 7.06 % showed ex-vacuo dilatation of the ventricles, 3.53% showed colpocephaly and 4.71 % showed other abnormalities.

Graph 20: Distribution According To Ventricular Abnormalities

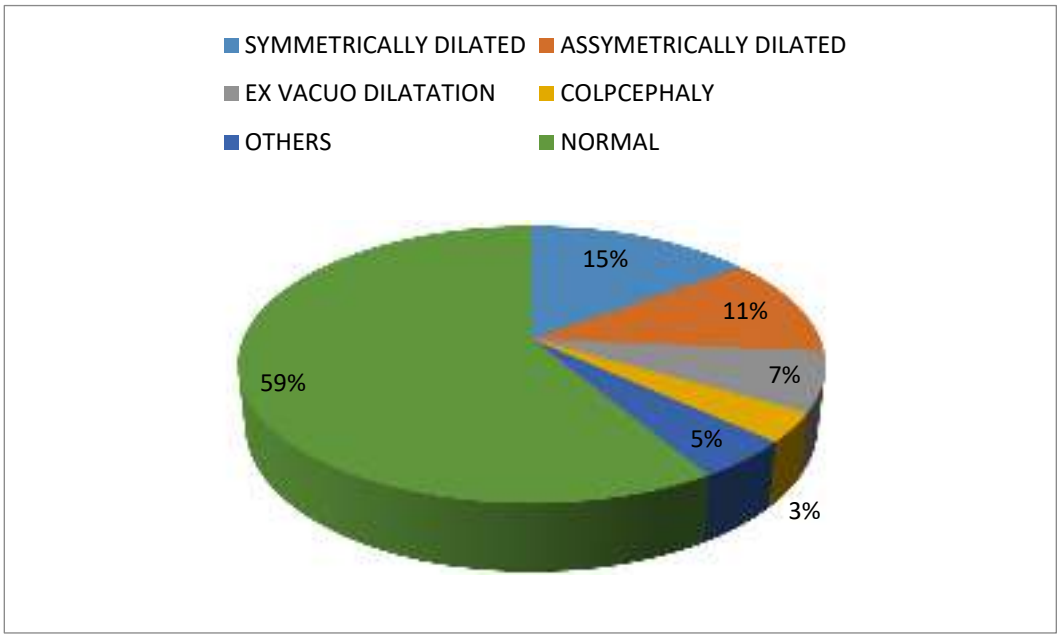


Table 21: Distibution According To Normal Or Abnormal Scpectroscopy

SPECTROSCOPY	NUMBER	PERCENTAGE
normal	**76**	**89.41**
abnormal	**9**	**10.59**

Only 10.59 % of the children who had normal MRI findings had abnormal findings on spectroscopy.

Graph 21: Distibution According To Normal Or Abnormal Scpectroscopy

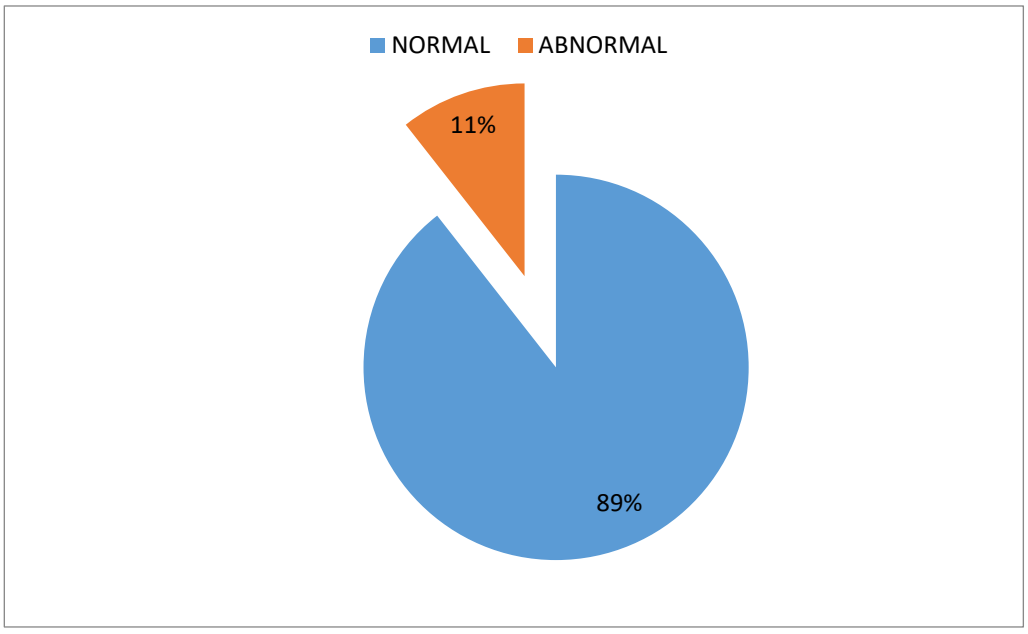


Table 22: Distribution According To Abnormal Findings In Spectroscopy

ABNORMALITY	NORMAL	PERCENTAGE
DECREASED NAA	4	44.44
INCREASED LACTATE	3	33.33
INCREASED CHOLINE	1	11.11
CREATININE PEAK	1	11.11

Amongst the children with abnormal spectroscopy finsdings , 44.44 % of the children had decreased NAA, 33.33 % had ncreased lactate and 11.11 % had increased choline or choline peak.

Graph 22: Distribution According To Abnormal Findings In Spectroscopy

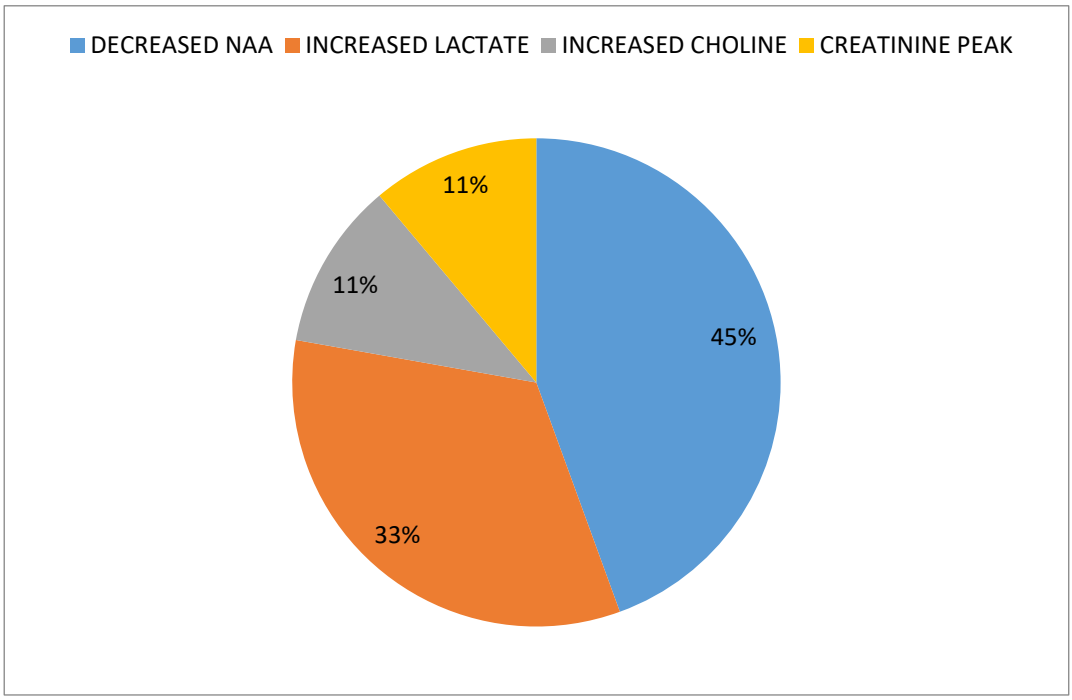


Table 23: Distribution According To Periventricular Leucomalacia

	NUMBER	PERCENTAGE
PVL PRESENT	**18**	**21.17**
PVL ABSENT	**67**	**78.28**

21.17% of the children had findings of perviventricularleucomalacia (PVL) imaging findings.

Graph 23: Distribution According To Periventricular Leucomalacia

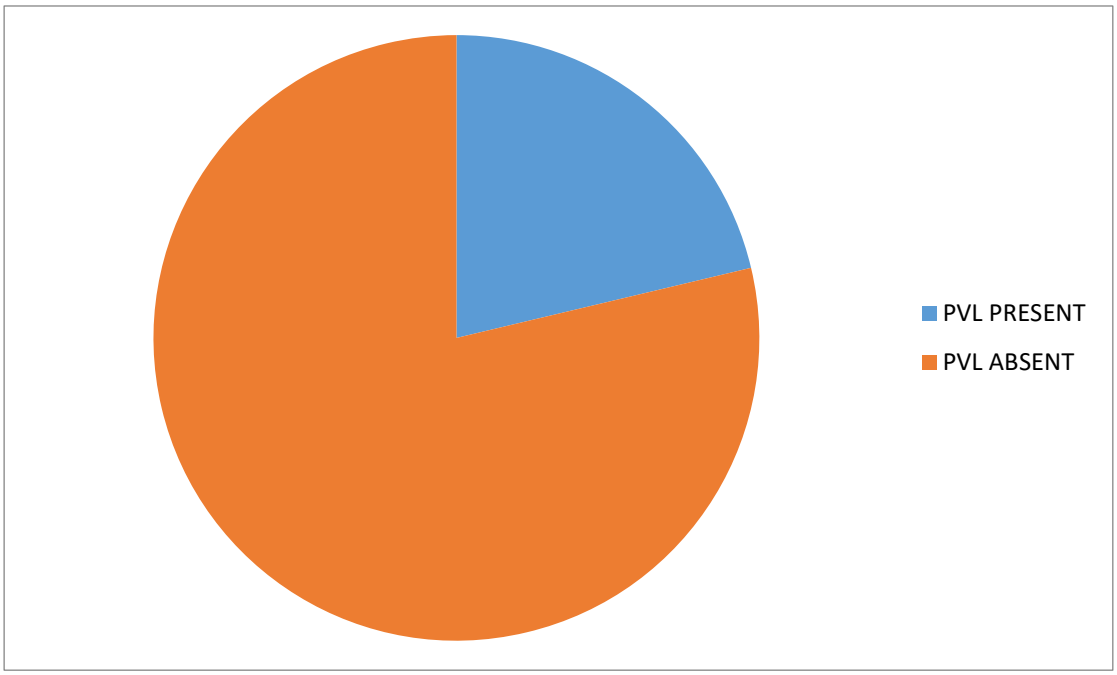
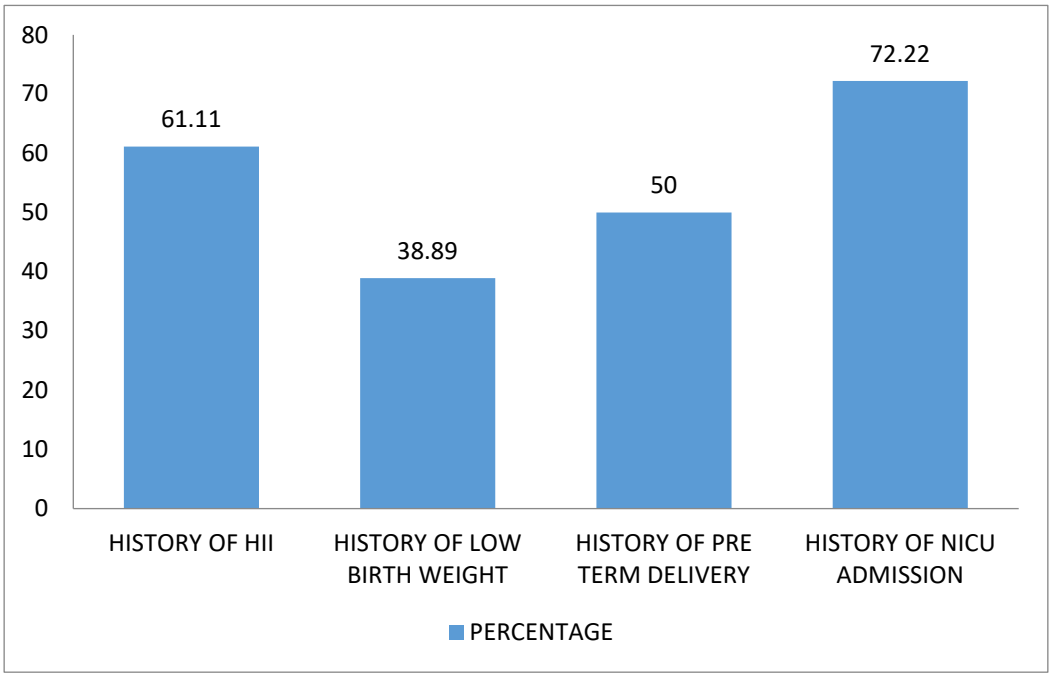


Table 24: Correlation of PVL with Past History (N-18)

PAST HISTORY	NUMBER	PERCENTAGE
HISTORY OF HII	11	61.11
HISTORY OF LOW BIRTH WEIGHT	7	38.89
HISTORY OF PRE TERM DELIVERY	9	50.0
HISTORY OF NICU ADMISSION	13	72.22

The children with imaging findings of perviventricularleucomalacia were distributed according to birth history. 61.11 % of the children out of these had history of hypoxic ischemic insult, majority of children also has historu of NICU admission, 38.89 % also had history of Low birth weight and 50 % had pre term deliver.

Graph 24: Correlation of PVL with Past History (N-18)



DISCUSSION

Role of MRI was studied in 85 patients presenting with complaints of developmental delay ranging from 2 months to 7 years. The majority of children in the study with abnormal MRI findings belonged to the 2 months to 12 months age group (31.15%), with the next two similar peaks being 1 to 3 years of age (29.51 %) and greater than 5 years of age (29.51%). Least number of children with abnormal MRI findings belonged to 3 to 5 years of age group (9.84%). In the study conducted by Ali et al [44] similar age presentation was seen with most of the patients with abnormal MRI belonging to 3 to 12 months of age (38%) with the next peak at 1-2 years (24%). This age distribution could be attributed to usual early detection of signs of developmental delay by the parents. Early detection of cases could help in earlier detection of cause and start of the treatment.

In our study males (69.41%) were significantly more in number than females (30.58%) . it was considerably different from the study conducted by Ali et al.,[44] Pranay & Chitnis, [101] , Dasan & Deepashree, [102] and Konde et al., [103] in which there was not much difference in the number of males and females. This significant sex difference could be contributed to be due to chance as there is no known correlation between sex and abnormal brain MRI.

Based on MRI findings the study population was divided into various etiological categories. Etiological classification showed congenital/developmental anomalies ranked highest in our study (25.88%), Traumatic/ Neurovascular Diseases (Hypoxic Ischemic Brain Injury) (18.82) and metabolic cause(18.82) ranked the second highest. Momen et al.[38], Konde et al., [103] and Ramya et al., [104] in their

studies had slightly different findings to our study in which (Hypoxic Ischemic Brain Injury ranked the highest followed by developmental / congenital anomalies. In these studies congenital and developmental anomalies ranked higher than metabolic and neurodegenerative disorders which is against what we have encountered in our study in which percentage of children having metabolic or traumatic /neurovascular cause were the highest.

This study had 23 cases (25.88%) of congenital and developmental anomalies, with few of them beings corpus callosal hypoplasia/ aplasia, cerebellar hypoplasia, lissencephaly-pachygyria spectrum, polymicrogyria. Cases of aicardi syndrome was also seen in this study. Tolba S et al [106] had reported incidence of congenital and developmental anomalies to be around 26% in their study whereas Konde et al., [103] and Ramya et al., [104] had reported lower incidence about 12.5% and 12% respectively as they had included children with history of trauma in their studies which was more or less excluded in ours.

Our study had 16 cases (18.82%) having MRI features suggestive of metabolic/degenerative etiology. Various different metabolic/degenerative cases which were seen in our study were neuronal ceroid lipofuscinosis, west syndrome, congenital disorder of glycosylation, landing syndrome, mitochondrial myopathy, biotinase deficience, tay-sachs disease and beta-1 gangliosisdosis.

3 cases of infectious etiology were seen in our study with 1 of them being a case of CMV infection palsy and 1 case showing features suggestive of changes of post meningitis with dilatation of ventricles on MRI. Tolba et al [106] had similar incidence in their study. Konde et al., [103] in his study had reported few cases with

features of infection (with incidence of 5%) like meningitis, encephalitis and cerebral abscess

Only one case of neoplastic etiology was seen in our study.(case 6) 6 month year old male child with complaints of right sided hemiplegia and no neck holding was found to have a space occupying lesion in the left temporal region. The lesion shows peripheral areas of restriction on DWI sequence and blooming on SWI sequence .The child was diagnosed to have astrocytoma. Konde et al in their study had reported 2 cases of posterior cranial fossa lesion. Tolba et al [107] had one case of recurrrant astocytoma.

72.94 % (62/85) of the children were clinically diagnosed to have cerebral palsy, out of which 72 .58 % (45/62) had abnormal MRI brain findings. 12.94 % (11/85) of the study population were diagnosed to have global developmental delay/ intellectual disability pattern of clinical presentation out of whom 63.63% (7/11) had abnormal MRI brain. Only 3.52 % (3/85) of the population had autism like clinical presentation. Rest of the study population (11.76 %) had other clinical diagnosis.

Out of the children 62 children diagnosed to have cerebral palsy, the most common type of cerebral palsy was found to be 72.58 % (45/62) spastic cerebral palsy (72.58%) with others showing lesser percentage of prevalence.

Based on clinical history it was found that 48.23% (41/85) of the population had presented only with developmental delay, and 51.76% (44/85) had presented with DD and other supplementary clinical symptoms like seizures, neurological insufficiency, gait disturbance, fever, weakness etc. the patients with developmental delay and additional features had higher yield with 77. 27 % (34/44) of these patients

showing abnormal MRI findings whereas 65.85 % of the patients with only developmental delay showing abnormal MRI brain findings. These results were similarly stated in study done by Aliet al. [44]

The children were carefully assessed based on past birth history. Patients having eventful birth history like LSCS delivery, pre term delivery , low birth weight, history of hypoxic insult or NICU admission showed higher yield as compared to children having normal birth history.

High diagnostic yield of abnormal MRI brain findings was found in our study in children with history of low birth weight, pre term deliver, history of hypoxic ischemic insult and history of NICU admission. Out of the 26 children who had history of low birth weight a majority of 80.85% (23/26) children showed abnormal findings. Out of the 20 children children who had history of pre term delivery around 80% of the children had abnormal findings . Out of the 58 children who had history of hypoxic insult , majority 48.23 % (41/85) had abnormal findings similarly , out of the 20/85 children who had history of NICU admission about 90 % of the children had abnormal findings. Similar findings were stated in the study by Ali et al [44] .Low diagnostic yield was associated with history of LSCS delivery and children who didn't cry immediately after birth. Out of 26 children of the study population having history of LSCS delivery,only 6.92% (18/26)had abnormal findings. Out of 40 children who had cried immediately after birth, 36.47 % had abnormal findings.

The study population was also studied for history of consanguineous marriage. 24 /85 (28.23%) had history of marriage within the family. Out of these 6/24(25%) had normal MRi brain findings and 18 / 24 (75%) had abnormal MRI brain findings. Out of these there were 18 abnormal slightly higher incidence of congenital/

developmental abnormality (44.44% (8/18)). Similar to our study, Momen et al[38] showed that there were slightly higher rate of congenital and developmental disease as the cause of developmental delay . This could be explained by increased rate of developmetal/ congenital abnormalities in related individuals who are married.

The study population was distributed based on relation to the head size, 84.70 % (72/85) of the children had normal head size. Only 5.88% (5/85) of the children had macrocephaly and only 9.41 % (8/85) had microcephaly. 75.0% of the children with microcephaly and 60.0 % of the children with macrocephaly had abnormal brain findings. Curry et al [100] had stated in their study that the yield of a imaging was amplified when it was done in occurrence of specific problems such as microcephaly, focal neurologic deficitor seizure disorder .Hence , MRI brain was recommended as a first-line investigation for patients with microcephaly, macrocephaly, seizures, abnormal neurological findings or abnormal birth history. Patients without these specific problems could postpone imaging until first-line genetic and metabolic investigations have been performed.

Out of the 85 patients selected for the study, abnormal findings on MRI brain were obtained in astounding 92.94 % of the patients, with 70.58 % of the patients having major abnormal findings and 22.35 % showing minor incidental findings. A range of previous studies have shown variation in the percentage of patients with abnormal findings on brain MRI. Momen et al [38] showed abnormal findings in 58.6% of patients, Ali AS et al., [44] in 68% , Koul et al in [5] 71.8% , Widjaja et al [43] in 84% and Bouhadiba et al.[107] in 48.6% The broad variation could be due to patient selection.

The 79 patients who had abnormal MRI findings were evaluated according to the anatomical structures involved. Different anatomical structures like cortical grey matter, white matter, medial temporal lobe, ventricles, basal ganglia, corpus callosum, brainstem and cerebellum were analysed. In this study majority of the patients had white matter abnormalities (excluding corpus callosum) (41.18%) and ventricles abnormalities (40%). Next peak was obtained with abnormalitites of corpus callosum (21%). similar results were obtained in previous studies conducted by Ali at al [44] in which abnormalities in ventricles (62%) and white matter were most common(58%). Widjaja et al.,[43] assessed 90 similar children and found that ventricles (48%) and CC (44%) were the most commonly involved structures. DECOBERT et al [97] had measured the value of MRI in DD and noticed white matter abnormalities in 15%, corpus callosal changes in 14% and ventricular abnormalities in 12% of the patients. Zeegers et al [71] had also assessed 45 children having developmental delay and autism and found abnormality in 49% of the children.

Similar to the study done by Ali et al [44] who had 22% of the cases showing incidental minor abnormalities like dilated VR spaces and mega cistern magna, our study showed 22.35% (19/85) of the patients had minor abnormities . Majority of the patients had enlarged subarachnoid spaces (42.35%), cavum septum pelucidum/ vergae /interpositum (25.88%) and mega cisterna magna (44.70), and dilated VR spaces (12.94%). Dilated VR spaces and enlarged sub-arachnoid spaces could be hypothesised to be due to brain atrophy occurring due to old parenchymal/vascular insult. They had noticed prominent VR spaces in 11% of their cases. Soto-Ares et al [70] had found enlargement of VR space in about 10% of their cases. Rollinset al.[98] had found a relationship linking the occurrence of dilated VR spaces and the occurrence of DD.

Among the 22 children (25.9%) who showed corpus callosal abnormalities, majority of them showed diffuse thinning 45.45%(10/22). Few of them showed asymmetrical thinning (9/22) with anterior thinning in 1 patient, posterior thinning in 4 cases and thinning of body in 4 cases .Only 3 cases showed complete agenesis, 1 showed abnormal orientation of the splenium of the corpus callosum and 1 case showed changes in signal abnormalities. Soto-Ares et al. [70] in his study had found corpus callosum abnormalities in large majority (46%) of the patients with mental retardation, like short or hypoplastic CC or vertical splenium. Zeegers et al.[71] had also seen alterations in the size and the shape of the CC in 9% (4/45) of the cases.

Atypical morphology of the CC has also been described in symptomatic children with MR .Thinning of the CC has been credited either to reduction in the number of axons traversing the CC or abnormal myelination. Abnormal morphology of the CC like vertical orientation of CC or drooping splenium of CC is hypothesised to be due to abnormal orientation of fibers of the CC that traverse through it. Filippi et al, [73] using diffusion tensor imaging had found increased diffusion constant and decreased anisotropy in the white matter, including the corpus callosum in children with developmental delay . Abnormal anisotropy could be due to failure of axonal growth or normal myelin development, which could effect in changes of the white matter tracts in the CC. Hence, usually additional studies would be required in these patients to assess the volume of white matter tracts by means of DTI.

Amongst the 25 cases showing abnormalities in the ventricles , 15.29% showed symmetrical dilatation of ventricles, 11.76% showed asymmetrical dilatation of the ventricles, 7.06 % showed ex-vacuo dilatation of the ventricles, 3.53% showed colpocephaly and 4.71 % showed other abnormalities. The alteration in size of the

ventricles may be indication of modification in the volume of white matter. For example loss of white matter could lead to dilatation of ventricles. Similarly, history of old ischemic /vascular injury would lead to gliosis of white matter and hence dilatation of ipsilateral ventricles. Likewise, enlargement of trigones of the lateral ventricles could be credited to deformity of the sagittal stratum.

Amongst the children with white matter abnormalities 22.86% of the children had showed diffuse T2 and FLAIR altered signal intensities, 22.86% had showed focal gliotic area in the white matter due to old hypoxic/vascular insult. 20% of the cases had showed focal area of altered T2 signal intensities and 17.14% had showed paucity of white mater. Lesser percentage of children (26%) had showed abnormalities of the white matter. In a study done by were. Out of those 26%, 65%had minor high T2 signal changes and 13% had diffuse white matter high T2 abnormalities. Soto-Ares et al. [70] had seen white matter abnormalities in even lesser percentage (10%) of patients, plus diffuse or patchy white matter abnormalities. Decombert et al. [97] had discovered that signal abnormalities in the peri-ventricular posterior WM are more probable to be seen in children with MR compared to the controls .The etiology of the white matter changes is still uncertain. It was hypothesised that the white matter abnormalities are related to changes in myelination. However our study had showed delayed myelination in 2.85% of the cases. Delayed myelination is more likely correlated to delay in the brain maturation.

Amongst the 10.59% of minority of children who had abnormal Spectroscopy findings, 4 of the cases had shown decreased NAA levels (with decreased NAA/Cr ratio, 3 cases had shown lactate peak , 1 case had shown choline peak with elevated Cho/Cr radio and 1 case had shown creatinine peak. FILIPPI et al [77] had found

decline in NAA/Cr and increase in Cho/Cr ratios in the white matter in parieto-occipital region and frontal region in 12 children with developmental delay having normal MR imaging. FAYED et al.[94] also had also stated lesser NAA/Cr ratio in 12 children with developmental delay who had normal MR compared to the healthy control subjects .They also stated that increasing the Cho/Cr ratio could revealing capability to integrate choline-containing molecules into myelin, or due to loss of normal myelin whereas the reduction in NAA/Cr ratio could be due to reduction in the quantity of normal neurons, hypomyelination, or decrease in synaptic density.

Limitations:

1. This study lacked a control group thus, there was a possibility that some of the findings that we considered abnormal, like enlarged subarachnoid spaces or assymetrical lateral ventricles could be seen in few normal children, but to a smaller degree.
2. In our study, we had a relatively huge age range including children ranging from 2 months to 7 years . There could be a possibility of finding more defects in the younger children , as they would be presenting prior for their imaging. In our study also we found more MR abnormalities in children less than 2 years than those more than 2 years

CONCLUSION

1. This study aimed to evaluate the role of MRI in children with developmental delay with clinical context conducted in the department of radio-diagnosis of tertiary care hospital. 85 patients were chosen by universal sampling

2. The diagnostic utility of imaging modalities like CT is limited in these children, but MRI has higher utility. In our study, the age of presentation of developmental delay varied. The most common clinical symptoms accompanying DD were seizures and abnormal posturing.

3. Patients with DD were evaluated with MRI and evaluated according to anatomical structure involved and the suspected etiological cause of symptoms.

4. Most common causes of developmental delay in our study was congenital /developmental anomalies , traumatic /neurovascular and metabolic was second highest

5. Only one case of neoplastic etiology was observed in our case study

6. 2 cases of infectious etiology were reported in our study.

7. Children with eventful birth history like pre term delivery and low birth weight showed higher yield as compared to children with normal birth history

8. Higher yield of MRI was found in our study in children with additional specific problems like microcephaly, macrocephaly, seizures etc

9. White matter, corpus callosum and ventricles were the most common structures involved in children with DD

10. Majority of the children were clinically diagnosed to have cerebral palsy

11. The patients with DD and additional features had higher yield than patients with only developmental delay .

SUMMARY

- A prospective study was conducted in the department of Radio-diagnosis of a tertiary care hospital to assess the role of MRI in the evaluation of children with DD.
- This study highlighted the role of MRI in guiding the clinician towards the etiology by its ability to diagnose congenital /developmental abnormalities and hypoxic ischemic injury with high precision.
- MRI along with spectroscopy had important role in diagnosing metabolic causes with certain imaging features that guide the clinician towards specific genetic and biochemical testing.
- MRI could be chosen as a first line investigation in patients with specific problems like microcephaly, seizures and neurological deficit as the yield of MRI was amplified in these cases.
- The study showed lesser role of spectroscopy in children with developmental delay if the routine MRI was normal.

BIBLIOGRAPHY

1. Williams HJ. Imaging the child with developmental delay. Imaging. 2004;16(2):174–185.

2. Swaiman KF. General aspects of patient neurologic history. In: Swaiman KF, Ashwell S, editors. Pediatric Neurology. 4th edition. Vol. 1. Philadelphia, Pa, USA: Mosby; 2006. pp. 1–14.

3. Shevel MI, Swaiman KF. GDDand mental retardation. In: Swaiman KF, Ashwell S, editors. Pediatric Neurology. 4th edition. Vol. 1. Philadelphia, Pa, USA: Mosby; 2006. pp. 551–567.

4. Frances P. Glascoe developmental screening and surveillance. In: Behrman RE, Kiegman RM, Jenson HB, editors. Nelson Text Book of Pediatrics. 18th edition. Vol. 16. Philadelphia, Pa, USA: Saunders; 2007. pp. 74–81.

5. Barkovich AJ, Kuzniecky RI, Jackson GD, Guerrini R, Dobyns WB. Classification system for malformations of cortical development: update 2001. Neurology. 2001;57(12):2168–2178.

6. Bellman M, Byrne O, Sege R. Developmental assessment of children. BMJ. 2013 Jan 15;346:e8687.

7. Choo YY, Agarwal P, How CH, Yeleswarapu SP. Developmental delay: identification and management at primary care level. Singapore Med J. 2019 Mar;60(3):119-123.

8. Vasudevan P, Suri M. A clinical approach to developmental delay and intellectual disability. Clin Med (Lond). 2017 Dec;17(6):558-561.

9. Eickmann SH, Emond AM, Lima M. Evaluation of child development: beyond the neuromotor aspect. J Pediatr (Rio J). 2016 May-Jun;92(3 Suppl 1):S71-83.

10. Salomone E, Pacione L, Shire S, Brown FL, Reichow B, Servili C. Development of the WHO Caregiver Skills Training Program for Developmental Disorders or Delays. Front Psychiatry. 2019;10:769.

11. Dornelas Lde F, Duarte NM, MagalhãesLde C. [Neuropsychomotor developmental delay: conceptual map, term definitions, uses and limitations]. Rev Paul Pediatr. 2015 Jan-Mar;33(1):88-103.

12. Vitrikas K, Savard D, Bucaj M. Developmental Delay: When and How to Screen. Am Fam Physician. 2017 Jul 01;96(1):36-43.

13. Kim YS, Leventhal BL, Koh YJ, Fombonne E, Laska E, Lim EC, Cheon KA, Kim SJ, Kim YK, Lee H, Song DH, Grinker RR. Prevalence of autism spectrum disorders in a total population sample. Am J Psychiatry. 2011 Sep;168(9):904-12.

14. Hatton C. Emerson E. Glover G, et al. People with learning disabilities in England 2013. London:: Public Health England; 2014.

15. Vitrikas K, Savard D, Bucaj M. Developmental Delay: When and How to Screen. Am Fam Physician. 2017 Jul 01;96(1):36-43.

16. Donald KA, Wedderburn CJ, Barnett W, Nhapi RT, Rehman AM, Stadler JAM, Hoffman N, Koen N, Zar HJ, Stein DJ. Risk and protective factors for child development: An observational South African birth cohort. PLoS Med. 2019 Sep;16(9):e1002920.

17. Meerding WJ, Bonneux L, Polder JJ, et al. Demographic and epidemiological determinants of healthcare costs in Netherlands: cost of illness study. BMJ 1998;317(7151):111–115. doi:10.1136/bmj.317.7151.111.

18. World Health Organization (WHO)(World report on disability. Geneva: World Health Organization, World Bank; 2011. Available from: http://www.who.int/disabilities/world_report/2011/rep ort.pdf. [Accessed on May 25, 2016].

19. Mackrides P S,Ryherd S J. Screening for developmental delay. Am Fam Physician 2011;84(5):544-9.

20. Boyle C, Boulet S, Schieve L, Cohen R, Blumberg S, Yeargin-Allsopp M et al. Trends in the Prevalence of Developmental Disabilities in US Children, 1997- 2008. Pediatrics 2011;127(6):1034-42. A Review of Developmental Delay and Its Determinants In Under Five Children National Journal of Medical and Allied Sciences | Vol 6 | Issue 2 | 2017 Page 70

21. Newacheck P, Strickland B, Shonkoff J, Perrin J, McPherson M, McManus M et al. An Epidemiologic Profile of Children With Special Health Care Needs. Pediatrics 1998;102(1):117-23.

22. Singh A, Kamble B, Gangwar K, Roy N. A Review of Developmental Delay and its Determinants in Under Five Children. National Journal of Medical and Allied Sciences 2017; 6 (2): 66-70

23. Nair M, George B, Padmamohan J, Sunitha R, Resmi V, Prasanna G, et al. in kerela among 12520 rural children which happens to be the largest sample size

compared to others). Develpomental delay and disability among under-5 children in a rural ICDS Block. Indian Pediatr. 2009;46:S75-S78

24. Jacob S K and Kumari K S. Developmental profile of children under two years in the coastal area Kochi, Kerala. Int J of Advanced Research 2013;1:870-4

25. Ali SS, Balaji, Dhaded SM, Goudar SS. Assessment of growth and global developmental delay: a study among young children in a rural community of India. Int Multidisciplinary Res J 2011,1:31-34

26. Vora H, Shah P, Mansuri S. A study on Developmental delay among children less than 2 year attending Well Baby Clinic - Prevalence and antecedents factors. Int J Med Sci Public Health 2013;2(4):1084-1087

27. Meenai Z, Longia S. A study on Prevalence & Antecedents of Developmental delay among Children less than 2 years attending Well Baby Clinic. Peoples J of Sci Res 2009;2(1):9-12

28. Routray S, Meher B, Tripathy R, Parida S, Mahilary N, Pradhan D. . Growth and development among Children Living in Orphanages of Odisha, an Eastern Indian State. IOSR Journal of Dental and Medical Sciences (IOSR-JDMS) 2015;14:38-41

29. Burnside RD, Pasion R, Mikhail FM, Carroll AJ, Robin NH, Youngs EL, Gadi IK, Keitges E, Jaswaney VL, Papenhausen PR, Potluri VR, Risheg H, Rush B, Smith JL, Schwartz S, Tepperberg JH, Butler MG. Microdeletion/ microduplication of proximal 15q11.2 between BP1 and BP2: a susceptibility region for neurological dysfunction including developmental and language delay. Hum Genet. 2011 Oct;130(4):517-28.

30. Miclea D, Peca L, Cuzmici Z, Pop IV. Genetic testing in patients with global developmental delay /intellectual disabilities. A review. Clujul Med. 2015;88 (3):288-92.

31. Hagerman RJ, Berry-Kravis E, Kaufmann WE, Ono MY, Tartaglia N, Lachiewicz A, Kronk R, Delahunty C, Hessl D, Visootsak J, Picker J, Gane L, Tranfaglia M. Advances in the treatment of fragile X syndrome. Pediatrics. 2009 Jan;123(1):378-90.

32. Moeschler JB, Shevell M., Committee on Genetics. Comprehensive evaluation of the child with intellectual disability or global developmental delays. Pediatrics. 2014 Sep;134(3):e903-18.

33. Bellman M, Byrne O, Sege R. Developmental assessment of children. BMJ. 2013 Jan 15;346:e8687.

34. Udagawa J, Hino K. Impact of Maternal Stress in Pregnancy on Brain Function of the Offspring. Nihon EiseigakuZasshi. 2016;71(3):188-194.

35. Ellis BJ, Boyce WT. Differential susceptibility to the environment: toward an understanding of sensitivity to developmental experiences and context. Dev Psychopathol. 2011 Feb;23(1):1-5.

36. Srour M, Mazer B, Shevell MI. Analysis of clinical features predicting etiologic yield in the assessment of global developmental delay. Pediatrics. 2006 Jul;118(1):139-45. doi: 10.1542/peds.2005-2702. PMID: 16818559.

37. T. Kaur, D. Sood, N.S. Chauhan, P.K. Soni AUR1 , D. SOOD , N. S. Chauhan , P. K. SONI ; MRI evaluation of brain in paediatric patients presenting with

developmental delay ,European society of radiology, ECR 2018 / C-1084, (DOI: 10.1594/ecr2018/C-1084)

38. Momen AA, Jelodar G, Dehdashti H. Brain Magnetic Resonance Imaging Findings in Developmentally Delayed Children. International Journal of Paediatrics. 2011 Article ID 386984.

39. Petersen MC, Kube DA, Palmer F B. Classification of developmental delays. Seminars in Pediatric Neurology. 1998;5(1):2–14.

40. Pandey A, Phadke SR, Gupta N, Phadke RV. Neuroimaging in mental retardation. Indian J Pediatr. 2004;71(3):203–09.

41. Koul R, Al-Yahmedy M, Al-Futaisi A. Evaluation children with global developmental delay: A prospective study at sultan qaboos university hospital, oman. Oman Medical Journal. 2012;27(4):310.

42. Battaglia A, Bianchini E, Carey JC. Diagnostic yield of the comprehensive assessment of developmental delay/mental retardation in an institute of child neuropsychiatry. American Journal of Medical Genetics. 1999;82(1):60–66.

43. Widjaja E, Nilsson D, Blaser S, Raybaud C. White matter abnormalities in children with idiopathic developmental delay. ActaRadiol. 2008;49(5):589–95.

44. Ali, A. S., Syed, N. P., Murthy, G. S., Nori, M., Abkari, A., Pooja, B. K., & Venkateswarlu, J. (2015). Magnetic resonance imaging (MRI) evaluation of developmental delay in pediatric patients. Journal of clinical and diagnostic research : JCDR, 9(1), TC21–TC24. https://doi.org/10.7860/JCDR/2015/11921.5478

45. Abdel Razek AA, Kandell AY, Elsorogy LG, Elmongy A, Basett AA. Disorders of cortical formation: MR imaging features. AJNR Am J Neuroradiol. 2009 Jan;30(1):4-11. doi: 10.3174/ajnr.A1223. Epub 2008 Aug 7. PMID: 18687750; PMCID: PMC7051699.

46. Pujol J, López-Sala A, Sebastián-Gallés N, Deus J, Cardoner N, Soriano-Mas C, Moreno A, Sans A. Delayed myelination in children with developmental delay detected by volumetric MRI. Neuroimage. 2004 Jun;22(2):897-903. doi: 10.1016/j.neuroimage.2004.01.029. PMID: 15193620.

47. Paus T, Collins DL, Evans AC, Leonard G, Pike B, Zijdenbos A. Maturation of white matter in the human brain: a review of magnetic resonance studies. Brain Res Bull. 2001 Feb;54(3):255-66. doi: 10.1016/s0361-9230(00)00434-2. PMID: 11287130.

48. van der Knaap, M.S., Valk, J., Bakker, C.J., Schooneveld, M., Faber, J.A.J., Willemse, J. and Gooskens, R.H.J.M. (1991), Myelination As An Expression Of The Functional Maturity Of The Brain. Developmental Medicine & Child Neurology, 33: 849-857. https://doi.org/10.1111/j.1469-8749.1991.tb14793.x

49. Mie Matsui, Chiaki Tanaka, LishaNiu, Kyo Noguchi, Warren B. Bilker, Michael Wierzbicki, Ruben C. Gur. Age-related Volumetric Changes of Prefrontal Gray and White Matter from Healthy Infancy to Adulthood. International Journal of Clinical and Experimental Neurology. 2016; 4(1):1-8. doi: 10.12691/ijcen-4-1-1.

50. Barkovich AJ, Kjos BO, Jackson DE Jr, Norman D. Normal maturation of the neonatal and infant brain: MR imaging at 1.5 T. Radiology. 1988 Jan;166(1 Pt 1):173-80. doi: 10.1148/radiology.166.1.3336675. PMID: 3336675.

51. Bird CR, Hedberg M, Drayer BP, Keller PJ, Flom RA, Hodak JA. MR assessment of myelination in infants and children: usefulness of marker sites. AJNR Am J Neuroradiol. 1989 Jul-Aug;10(4):731-40. PMID: 2505502; PMCID: PMC8332614.

52. Dietrich RB, Bradley WG, Zaragoza EJ 4th, Otto RJ, Taira RK, Wilson GH, Kangarloo H. MR evaluation of early myelination patterns in normal and developmentally delayed infants. AJR Am J Roentgenol. 1988 Apr;150(4):889-96. doi: 10.2214/ajr.150.4.889. PMID: 2450448.

53. Staudt M, Krägeloh-Mann I, Grodd W. Die normaleMyelinisierung des kindlichenGehirns in der MRT--eineMetaanalyse [Normal myelination in childhood brains using MRI--a meta analysis]. Rofo. 2000 Oct;172(10):802-11. German. doi: 10.1055/s-2000-7898. PMID: 11111291.

54. McArdle CB, Richardson CJ, Nicholas DA, Mirfakhraee M, Hayden CK, Amparo EG. Developmental features of the neonatal brain: MR imaging. Part I. Gray-white matter differentiation and myelination. Radiology. 1987 Jan;162(1 Pt 1):223-9. doi: 10.1148/radiology.162.1.3786767. PMID: 3786767.

55. De Bellis MD, Keshavan MS, Beers SR, Hall J, Frustaci K, Masalehdan A, Noll J, Boring AM. Sex differences in brain maturation during childhood and

adolescence. Cereb Cortex. 2001 Jun;11(6):552-7. doi: 10.1093/cercor/11.6.552. PMID: 11375916.

56. Giedd, J. N., &Rapoport, J. L. (2010). Structural MRI of pediatric brain development: what have we learned and where are we going?. Neuron, 67(5), 728–734. https://doi.org/10.1016/j.neuron.2010.08.040

57. Gur, R. C., Turetsky, B. I., Matsui, M., Yan, M., Bilker, W., Hughett, P., &Gur, R. E. (1999). Sex differences in brain gray and white matter in healthy young adults: correlations with cognitive performance. The Journal of neuroscience : the official journal of the Society for Neuroscience, 19(10), 4065–4072. https://doi.org/10.1523/JNEUROSCI.19-10-04065.1999

58. Iwasaki, N., Hamano, K., Okada, Y. et al. Volumetric quantification of brain development using MRI. Neuroradiology 39, 841–846 (1997). https://doi.org/10.1007/s002340050517

59. Pfefferbaum A, Mathalon DH, Sullivan EV, Rawles JM, Zipursky RB, Lim KO. A quantitative magnetic resonance imaging study of changes in brain morphology from infancy to late adulthood. Arch Neurol. 1994 Sep;51(9):874-87. doi: 10.1001/archneur.1994.00540210046012. PMID: 8080387.

60. Sowell, E. R., Johnson, A., Kan, E., Lu, L. H., Van Horn, J. D., Toga, A. W., O'Connor, M. J., &Bookheimer, S. Y. (2008). Mapping white matter integrity and neurobehavioral correlates in children with fetal alcohol spectrum disorders. The Journal of neuroscience : the official journal of the Society for

Neuroscience, 28(6), 1313–1319. https://doi.org/10.1523/JNEUROSCI.5067-07.2008

61. Thomson, C. E., McCulloch, M., Sorenson, A., Barnett, S. C., Seed, B. V., Griffiths, I. R., & McLaughlin, M. (2008). Myelinated, synapsing cultures of murine spinal cord--validation as an in vitro model of the central nervous system. The European journal of neuroscience, 28(8), 1518–1535. https://doi.org/10.1111/j.1460-9568.2008.06415.x

62. Golestani N, Molko N, Dehaene S, LeBihan D, Pallier C. Brain structure predicts the learning of foreign speech sounds. Cereb Cortex. 2007 Mar;17(3):575-82. doi: 10.1093/cercor/bhk001. Epub 2006 Apr 7. PMID: 16603709.

63. Penhune VB, Zatorre RJ, MacDonald JD, Evans AC. Interhemispheric anatomical differences in human primary auditory cortex: probabilistic mapping and volume measurement from magnetic resonance scans. Cereb Cortex. 1996 Sep-Oct;6(5):661-72. doi: 10.1093/cercor/6.5.661. PMID: 8921202.

64. Kara Murias, Andrea Moir, Kenneth Alexis Myers, Irene Liu, Xing-Chang Wei, Systematic review of MRI findings in children with developmental delay or cognitive impairment, Brain and Development,Volume 39, Issue 8, 2017, Pages 644-655, ISSN 0387-7604, https://doi.org/10.1016/j.braindev.2017.04.006.

65. Filippi CG, Uluğ AM, Deck MD, Zimmerman RD, Heier LA. Developmental delay in children: assessment with proton MR spectroscopy. AJNR Am J Neuroradiol. 2002 May;23(5):882-8. PMID: 12006297; PMCID: PMC7974746.

66. Verma A, Sagar NC, Kumar A, Srivastava A. Diagnostic value of diffusion tensor imaging derived metrics as biomarkers of cerebral changes in developmental delay. Indian J Radiol Imaging. 2015 Oct-Dec;25(4):415-20. doi: 10.4103/0971-3026.169457. PMID: 26752821; PMCID: PMC4693391.

67. Barkovich AJ, Norman D. Anomalies of the corpus callosum: correlation with further anomalies of the brain. AJR Am J Roentgenol. 1988 Jul;151(1):171-9. doi: 10.2214/ajr.151.1.171. PMID: 3259802.

68. Zimmerman RA, Bilaniuk UT, Gusnard DA. Pediatric cerebral anomalies. In: Stark 00, Bradley WG Jr. eds. Magnetic resonance imaging, vol. 1, 2nd ed. St. Louis: Mosby-Yean Book, 1992:1029-1 056 14. Jinkins JR. Whittemone AR, Bradley WG. MR imaging of callosal and conticocallosaldysgenesis. AJNR 1 989; 10:339-344

69. Jinkins JR, Whittemore AR, Bradley WG. MR imaging of callosal and corticocallosal dysgenesis. AJNR Am J Neuroradiol. 1989 Mar-Apr;10(2):339-44. PMID: 2494854; PMCID: PMC8331395.

70. Soto-Ares G, Joyes B, Lemaître MP, Vallée L, Pruvo JP. MRI in children with mental retardation. PediatrRadiol. 2003 May;33(5):334-45. doi: 10.1007/s00247-003-0891-z. Epub 2003 Mar 11. PMID: 12695867.

71. Zeegers M, Van Der Grond J, Durston S, Nievelstein RJ, Witkamp T, Van Daalen E, et al.Radiological findings in autistic and developmentally delayed children.Brain Dev 2006;28:4959.

72. 72.Gabrielli O, Coppa GV, Manzoni M, Carloni I, Kantar A, Maricotti M, et al.Minor cerebral alterations observed by magnetic resonance imaging in syndromic children with mental retardation.Eur J Radiol 1998;27:13944.

73. Filippi CG, Lin DD, Tsiouris AJ, Watts R, Packard AM, Heier LA, et al.Diffusion-tensor MR imaging in children with developmental delay: preliminary findings. Radiology 2003;229:4450.

74. Imamura T, Ariga H, Kaneko M, Watanabe M, Shibukawa Y, Fukuda Y, Nagasawa K, Goto A, Fujiki T. Neurodevelopmental outcomes of children with periventricular leukomalacia. PediatrNeonatol. 2013 Dec;54(6):367-72. doi: 10.1016/j.pedneo.2013.04.006. Epub 2013 May 30. PMID: 23727042.

75. Deng W, Pleasure J, Pleasure D. Progress in periventricular leukomalacia. Arch Neurol. 2008 Oct;65(10):1291-5. doi: 10.1001/archneur.65.10.1291. PMID: 18852342; PMCID: PMC2898886.

76. Volpe JJ. Cerebral white matter injury of the premature infant-more common than you think. Pediatrics. 2003 Jul;112(1 Pt 1):176-80. doi: 10.1542/ peds. 112.1.176. PMID: 12837883.

77. Filippi CG, Ulug AM, Deck MD, Zimmerman RD, Heier LA. Developmental delay in children: assessment with proton MR spectroscopy. Am J Neuroradiol 2002; 23:882 –888

78. Angelie E, Bonmartin A, Boudraa A, Gonnaud PM, Mallet JJ, Sappey-Marinier D. Regional differences and metabolic changes in normal aging of human brain: proton MR spectroscopic imaging study. Am J Neuroradiol 2001; 22:119 –127.

79. Hashimoto T, Tayama M, Miyazaki M, et al. Developmental brain changes investigated with proton magnetic resonance spectroscopy. Dev Med Child Neurol 1995; 37:398–405

80. Pouwels PJ, Brockmann K, Kruse B, et al. Regional age dependence of human brain metabolites from infancy to adulthood as detected by quantitative localized proton MRS. Pediatr Res 1999; 46:474–485.

81. Charles HC, Lazeyras F, Krishnan KR, et al. Proton spectroscopy of human brain: effects of age and sex. ProgNeuropsychopharmacolBiol Psychiatry 1994; 18:995 –1004.

82. Van der Voorn JP, Pouwels PJ, Hart AA, et al. Childhood white matter disorders: quantitative MR imaging and spectroscopy. Radiology 2006; 241:510–517

83. Verbruggen KT, Meiners LC, Sijens PE, et al. Magnetic resonance imaging and proton magnetic resonance spectroscopy of the brain in the diagnostic evaluation of developmental delay. Eur J PaediatrNeurol 2009; 13:181 –190.

84. Weiss U, Bacher R, Vonbank H, Kemler G, Ling A, Marksteiner J. Cognitive impairment: assessment with brain magnetic resonance imaging and proton magnetic resonance spectroscopy. J Clin Psychiatry 2003; 64:235 –242.

85. Vythilingam M, Charles HC, Tupler LA, Blitchington T, Kelly L, Krishnan KR. Focal and lateralized subcortical abnormalities in unipolar major depressive disorder: an automated multivoxel proton magnetic resonance spectroscopy study. Biol Psychiatry 2003; 54:744–750.

86. Levitt JG, O'Neill J, Blanton RE, et al. Proton magnetic resonance spectroscopic imaging of the brain in childhood autism. Biol Psychiatry 2003; 54:1355 –1366.

87. Alkan A, Sarac K, Kutlu R, et al. Proton MR spectroscopy features of normal appearing white matter in neurofibromatosis type 1. MagnReson Imaging 2003; 21:1049 –1053

88. American Journal of Roentgenology. 2010;194: 1110-1115. 10.2214/AJR.09.3204.

89. Rajvanshi N, Bhakat R, Saxena S, Rohilla J, Basu S, Nandolia KK, Agrawal S, Bhat NK, Chacham S. Magnetic Resonance Spectroscopy in Children With Developmental Delay: Time to Look Beyond Conventional Magnetic Resonance Imaging (MRI). J Child Neurol. 2021 May;36(6):440-446. doi: 10.1177/0883073820978006. Epub 2020 Dec 11. PMID: 33305985.

90. Filippi CG, Uluğ AM, Deck MD, Zimmerman RD, Heier LA. Developmental delay in children: assessment with proton MR spectroscopy. AJNR Am J Neuroradiol. 2002 May;23(5):882-8. PMID: 12006297; PMCID: PMC7974746

91. Chellathurai, Amarnath&Ramaswami, Sukumar& Xavier, Sebastian & A, Thangalakshmi&Kannappan, Sivakumar&Ayyamperumal, Balaji. (2018). Magnetic Resonance spectroscopy in children with non acute neurological illnes. Journal of Evolution of Medical and Dental Sciences. 7. 2481-2486. 10.14260/jemds/2018/558.

92. Verbruggen, K. T., Meiners, L. C., Sijens, P. E., Lunsing, R. J., van Spronsen, F. J., &Brouwer, O. F. (2009). Magnetic resonance imaging and proton magnetic resonance spectroscopy of the brain in the diagnostic evaluation of developmental delay. European Journal of Paediatric Neurology, 13(2), 181-190. https://doi.org/10.1016/j.ejpn.2008.04.014

93. Augustine, E., Spielman, D., Barnes, P. et al. Can magnetic resonance spectroscopy predict neurodevelopmental outcome in very low birth weight preterm infants?. J Perinatol 28, 611–618 (2008). https://doi.org/10.1038/jp.2008.66

94. Fayed N, Morales H, Modrego PJ, Muñoz-Mingarro J. White matter proton MR spectroscopy in children with isolated developmental delay: does it mean delayed myelination? AcadRadiol. 2006 Feb;13(2):229-35. doi: 10.1016/j.acra.2005.10.016. PMID: 16428059.

95. Krijn T. Verbruggena, *, Linda C. Meinersb , Paul E. Sijensb , Roelineke J. Lunsingc , Francjan J. van Spronsena , Oebele F. Brouwerceuropean journal of paediatric neurology 13 (2009) 181–190

96. Shafi RMA, VandeVoort JL, Croarkin PE, Romanowicz M. Parent-Child Interaction Therapy in a Case of Global Developmental Delay and Leukoencephalopathy. Front Psychiatry. 2018;9:427.

97. Decobert F, Grabar S, Merzoug V, Kalifa G, Ponsot G, Adamsbaum C, et al.Unexplained mental retardation: is brain MRI useful? PediatrRadiol 2005;35:58796.

98. Rollins NK, Deline C, MorrissMC.Prevalence and clinical significance of dilated Virchow-Robin spaces in childhood.Radiology 1993;189:537.

99. Gabrielli O, Coppa GV, Manzoni M, Carloni I, Kantar A, Maricotti M, et al.Minor cerebral alterations observed by magnetic resonance imaging in syndromic children with mental retardation.Eur J Radiol 1998;27:13944.

100. Curry CJ, Stevenson RE, Aughton D, Byrne J, Carey JC, Cassidy S, et al.Evaluation of mental retardation: recommendations of a consensus conference: American College of Medical Genetics.Am J Med Genet 1997;72:46877.

101. Pranay D.I. and Chitnis D.A.: Evaluation of children with developmental delay using MRI. Paripex-Indian Journal of Research, Vol. 6 Issue 1, p. 9-11, 2018.

102. Dasan T.A. and Deepashree B.: The Role of Brain Magnetic Resonance Imaging in the Evaluation of Children with Global Developmental Delay In: International Journal of Anatomy, Radiology and Surgery; 2016.

103. Kondre S.R., Sasane A, Jagtap P.R. and Bhole P.R.: MR imaging of the brain in children with developmental delay. Indian Journal of Applied Research, 7 (7): 46-8, 2018.

104. Ramya K., Sulaiman F.A.B. and Ashvind D.: MRI Evaluation of Brain in Developmental Delay Children, 2018.

105. Bouhadiba Z, Dacher J N, Monroc M, Vanhulle C, Menard J F, Kalifa G. MRI of the brain in the evaluation of children with developmental delay. Journal de Radiologie. 2000; 81: 870–73.

106. M.D., TOLBA & M.D., NADIA. (2020). Role of Brain Magnetic Resonance Imaging in Assessment of Pediatric Developmental Delay. The Medical Journal of Cairo University. 88. 115-124. 10.21608/mjcu.2020.93968.

ANNEXURE I – CONSENT FORM

KAHER,
J. N. MEDICAL COLLEGE, BELAGAVI
DEPT. OF RADIODIAGNOSIS
TITLE OF THE STUDY: "ROLE OF MAGNETIC RESONANCE IMAGING OF BRAININ EVALUATION OF CHILDREN WITH GLOBAL DEVELOPMENTAL DELAY- ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY"

INVESTIGATOR: Dr. Khyati Sharma GUIDE: _____

CO-GUIDE: _____

INTRODUCTION AND PURPOSE:

The cause of developmental delay frequently is unknown, and clinicians and families can be frustrated by the lack of neuroimaging correlation especially when considering therapeutic options and long-term prognosis. MRI can be used to elucidate the cause of delay, contribute to the long term functional outcome for these children and be included in the diagnostic algorithm as part of the neuroradiological assessment.

PROCEDURE:

I request you to kindly participate in the study titled study **"ROLE OF MAGNETIC RESONANCE IMAGING OF BRAIN IN EVALUATION OF CHILDREN WITH GLOBAL DEVELOPMENTAL DELAY- ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY"** at Dr. PrabhakarKore charitable hospital and Medical Research Centre, Belagavi" is being conducted by _____, post graduate in Radio diagnosis at J. N. Medical College Belagavi[, Karnataka, under the guidance of Dr.Rajendra Mali, Professor, Dept. of Radio diagnosis, J. N. Medical College, Belagavi.

We request you to participate in this study as you are eligible to be included. During the study you will be asked questions regarding your present and past medical history and you will be required to answer to the best of your knowledge. You will also be clinically examined as per the protocol drawn.

If you agree to participate in the study, please furnish the details pertaining to the study.

BENEFITS:

- Noninvasive modality

COMPLICATIONS:

- No risk to the patient has been documented from MRI imaging of the brain earlier.

ALTERNATIVES:

If you are not willing to take part in the study, your treatment or any other further investigations the patient wants to undergo, in future, in KLE Hospital will not be affected by your decision.

VOLUNTARY PARTICIPATION/WITHDRAWAL:

Taking part in this study is voluntary. You may choose not to take part in this study, or if I decide to take part I can later change my mind and withdraw from the study. You decision will not change the present or future health care or other services that you receive. The investigator or the sponsor may stop my participation in this study. I will tell if any important new findings that may change my willingness to continue to take part. If you choose not to take part in the study I will receive the standard treatment for patients with my condition.

COSTS:

NIL (The study is to be conducted on the participants who are advised MRI as a investigation for global developmental delay by the referring consultant and the participants will bear the charges for it.)

Payment for Participation: No incentive will be paid to you for participating in this study.

COMPENSATION:

In the event that you become injured as a result of taking part in this study, treatment whatever available at KLE hospital, Belagavi, will be offered to me. No reimbursement, compensation or free medical care is given to you.

CONFIDENTIALITY:

All information collected about you during the course of the study will be kept confidential to the extent permitted by the law. The code numbers will identify you in this research record. Information from this study may be published but your personal identity will be confidential in any publication/presentation.

QUESTION:

If any enquiries in the future or in case of research related injury illness, you may contact following person.

Dr. RoopaBellad
Professor
Chairman,
J.N. Medical College Institutional
Ethical
Committee for Human
Subjects Research
Ph. No: 0831-2473777,
Ext. 1529

CONSENT TO PARTICIPATE IN RESEARCH STUDY:

1. I understand that I am participating in the study, which includesmulti-parametric Magnetic Resonance Imaging of prostate.
2. I confirm that I have read and understood the information in the patient information sheet. Procedure is explained to me in detail along with information about the advantages and disadvantages of taking part in the study. I have been given the opportunity to discuss all aspects of the trial, to ask questions and hereby consent to participation in the trial outlined above.
3. I understand that the decision to take part in this study is completely voluntary and I am aware that I can choose to withdraw from the study at any point of time.
4. I consent to the photographing or recording of the procedure to be performed including appropriate portions of my body, for medical, scientific or educational purposes provided my identity is not revealed in the pictures or by the descriptive texts accompanying them.
5. I understand that there is no significant risk involved in the test that would be done in this study.
6. No guarantee or assurance has given by anyone as to the results that may be obtained.
7. My signature on this form signifies that I have willingly decided to participate after understanding the above information.

Participant's Name/ legally authorized _____

representative

Signature _____

Name and signature of witness _____

Name and signature of interviewer _____

Date:

Place:

ANNEXURE II : ETHICAL CLEARANCE

K.L.E. ACADEMY OF HIGHER EDUCATION AND RESEARCH
(Deemed - to- be- University)
Accredited 'A' Grade by NAAC (2nd Cycle) Placed in Category 'A' by MHRD (GoI)
JAWAHARLAL NEHRU MEDICAL COLLEGE,
NEHRU NAGAR, BELAGAVI-590010 (KARNATAKA-INDIA)
Website: http://www.jnmc.edu
E-Mail : dome@jnmc.edu
Phone: (+ 91-(0)831 Office : 2472550
Principal: 2471701
Fax No. +91 (0)831 – 2470759

Ref: MDC/DOME/ 285 Date: 24/12/2019

To.

REG NO. BS0119005
PG student in Radio-diagnosis,
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 **"ROLE OF MAGNETIC RESONANCE IMAGING OF BRAIN IN EVALUATION OF CHILDREN WITH GLOBAL D3EVELOPEMENTAL DELAY – ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY"**, is ethical and justifiable. The proposed research project has been cleared by the JNMC Institutional Ethics Committee on Human Subjects Research.

(Dr. Anita Dulal)
Member Secretary
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

(Dr. Roopa M Belhad)
Chairman,
JNMC Institutional Ethics Committee
on Human Subjects Research,
J.N.Medical College, Belagavi.

116

ANNEXURE III -PROFORMA

DATA COLLECTION INSTRUMENT

ROLE OF MRI BRAIN IN EVALUTION OF CHILDREN WITH DEVELOPMENTAL DELAY - A ONE YEAR HOSPITAL BASED CROSS SECTIONAL STUDY"

PATIENT DATA

SL.NO.		**DATE**	
PATIENT NAME		**MRI SCAN NO.**	
AGE		**SEX**	

HISTORY

SYMPTOMS	
PRESENTING SYMPTOMS: **DEVELOPMENTAL DELAY** **SEIZURES** **FEVER** **ABNORMAL POSTURING**	 **YES/NO** **YES/NO**
HISTORY OF PRESENTING ILLNESS: **PAST HISTORY OF SEIZURES:** **PAST HISTORY OF ABNORMAL POSTURING** **PAST HISTORY OF FEVER**	 **YES/NO** **YES/NO** **YES/NO**

BIRTH HISTORY: **CESAREAN DELIVERY:** **LOW BIRTH WEIGHT:** **PRE-TERM:** **CRIED IMMEDIATELY AFTER BIRTH(CIAB):** **HISTORY OF HYPOXIC INSULT** **HISTORY OF NICU ADMISSION:**	 **YES/NO** **YES/NO** **YES/NO** **YES/NO** **YES/NO** **YES/NO** **YES/NO** **YES/NO** **YES/NO**
HISTORY OF IMMUNIZATION	**YES/NO**
HISTORY OF BREAST FEEDING	**YES/NO**
HISTORY OF CONSANGUINEOUS MARRIAGE:	**YES/NO**

ABNORMAL HEAD SIZE **(MICROCEPHALY/MICROCEPHALY)**	**YES/NO**

CLINICAL DIAGNOSIS :(CEREBRAL PALSY/ INTELLECTUAL DISABILITY/ AUTISM):

MRI FINDINGS:

ABNORMALITY IN CORTICAL GREY MATTER	NORMAL/ABNORMAL
ABNORMALITY IN WHITE MATTER	NORMAL/ABNORMAL
ABNORMALITY IN MEDIAL TEMPORAL LOBE	NORMAL/ABNORMAL
ABNORMALITY IN VENTRICLES	NORMAL/ABNORMAL
ABNORMALITY IN BASAL GANGLIA	NORMAL/ABNORMAL
ABNORMALITY IN CORPUS CALLOSUM	NORMAL/ABNORMAL
ABNORMALITY IN BRAINSTEM	NORMAL/ABNORMAL
ABNORMALITY IN CEREBELLUM	NORMAL/ABNORMAL
DELAYED MYELINATION	NORMAL/ABNORMAL
MEGA CISTERNA MAGNA	NORMAL/ABNORMAL
DILATED VR SPACES	NORMAL/ABNORMAL
INTRA PARENCHYMAL CYSTS	NORMAL/ABNORMAL
CAVUM SEPTUM PELLUCIDUM/INTERPOSITI/VERGAE	NORMAL/ABNORMAL
ENLARGED SUB ARACHNOID SPACE	NORMAL/ABNORMAL
OTHER SIGNIFICANT FINDINGS, IF ANY	NORMAL/ABNORMAL

FINDINGS ON T1W	YES/NO
FINDINGS ON T2W	YES/NO
FINDINGS ON FLAIR	YES/NO
FINDINGS ON DIFFUSION	YES/NO
FINDINGS ON SWI IMAGES	YES/NO

FINDINGS on spectroscopy:

DECREASED NAA	PRESENT/ABSENT
INCREASED LACTATE	PRESENT/ABSENT
INCREASED CHOLINE	PRESENT/ABSENT
CREATININE PEAK	PRESENT/ABSENT

ANNEXURES IV: CASES

CASE 1 :

A 2.5 year old child presenting with delayed milestone , coarse facial features was clinically suspected to be GM1 gangliosidosis. Patient was preterm, lowbirthweight , had LSCS delivery and history of NICU admission and respiratory distress. MRI had features of hypoxic ischemic injury with paucity of white matter with T2 and FLAIR hyper intensities and asymmetrical dilatation of ventricles. However additional findings like macrocerebellum and mild dysplasia of cerebellum were inconsistent with features of hypoxic ischemic injury. Bilateral globuspallidi shows increased T2 and FLAIR hyperintensities.

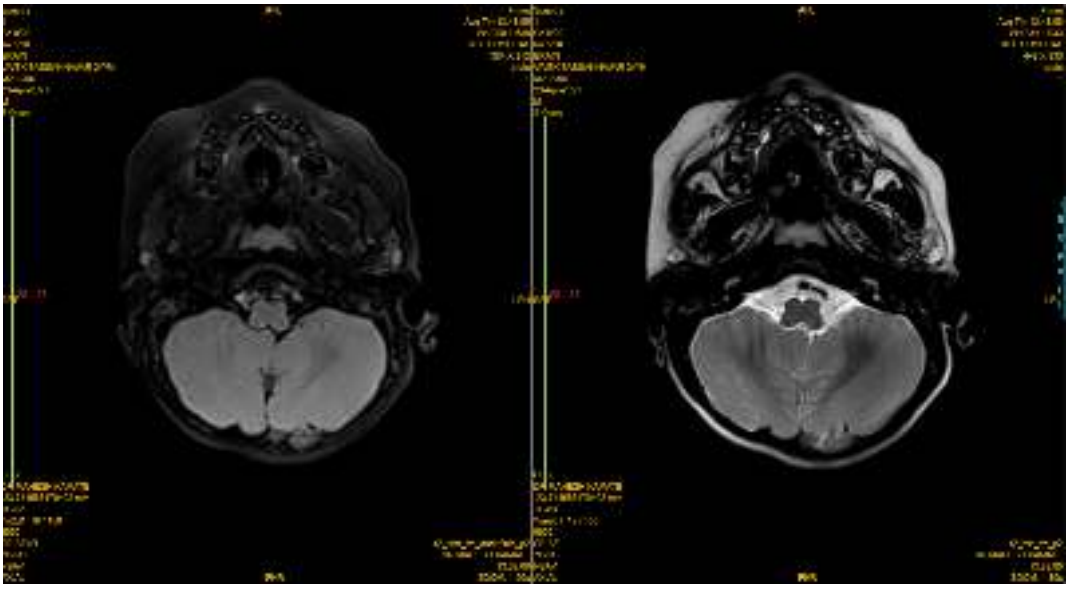


Fig 1.1 &1.2 : T2 weighted Axial images showing macrocerebelum and cerebellar dysplasia in right cerebellar lobe

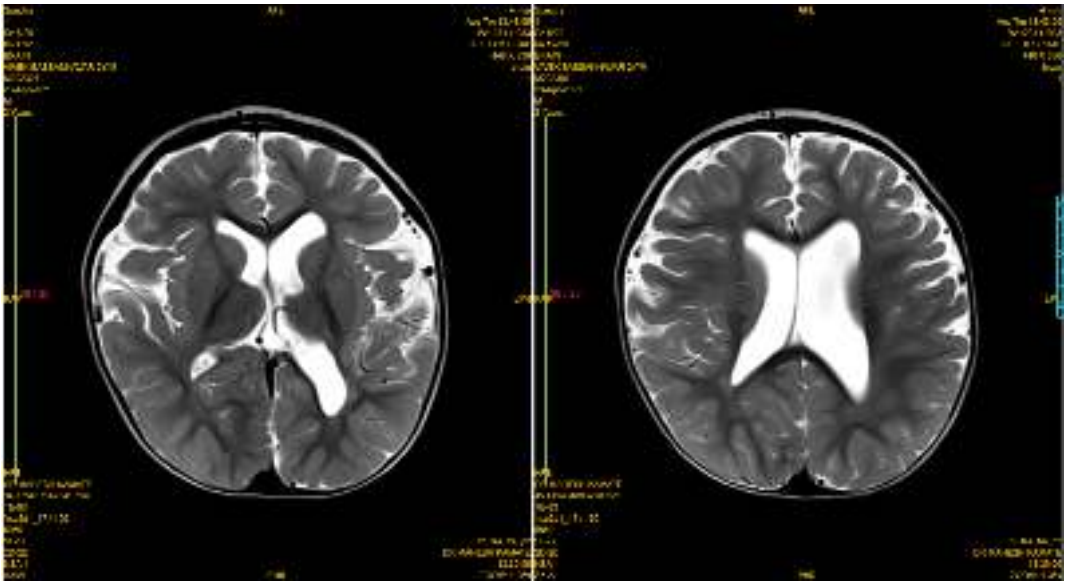


Figure 1.3 &1.4 Axial T2 weighted images showing paucity of white matter and asymmetrical dilatation of ventricles

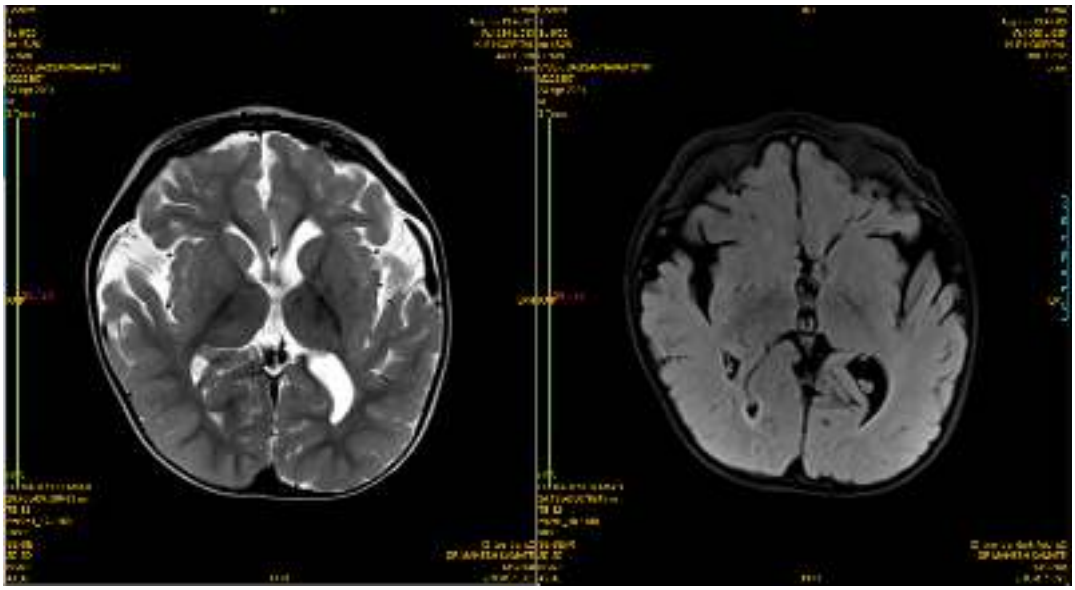


Figure 1.5 &1.6 Axial T2 weighted and FLAIR imagesshowing increased hypo-intensity in bilateral globipallidi

CASE 2:

A 2 year old child who presented with developmental delay , seizures and breathing difficulty at 2 years of age , the child also had progressive scoliosis as an incidental finding. History of consanguineous marriage was present. On getting MRI brain done, atrophy of midbrain and pons was seen resulting in figure of 8 pons appearance. The splenium of corpus callosum was vertical in orientation . Mild prominence of prepontine ,quadrigeminal and cerebellar cistern was noted. the boy was finally diagnosed with pitt Hopkins syndrome with TGF gene mutation.

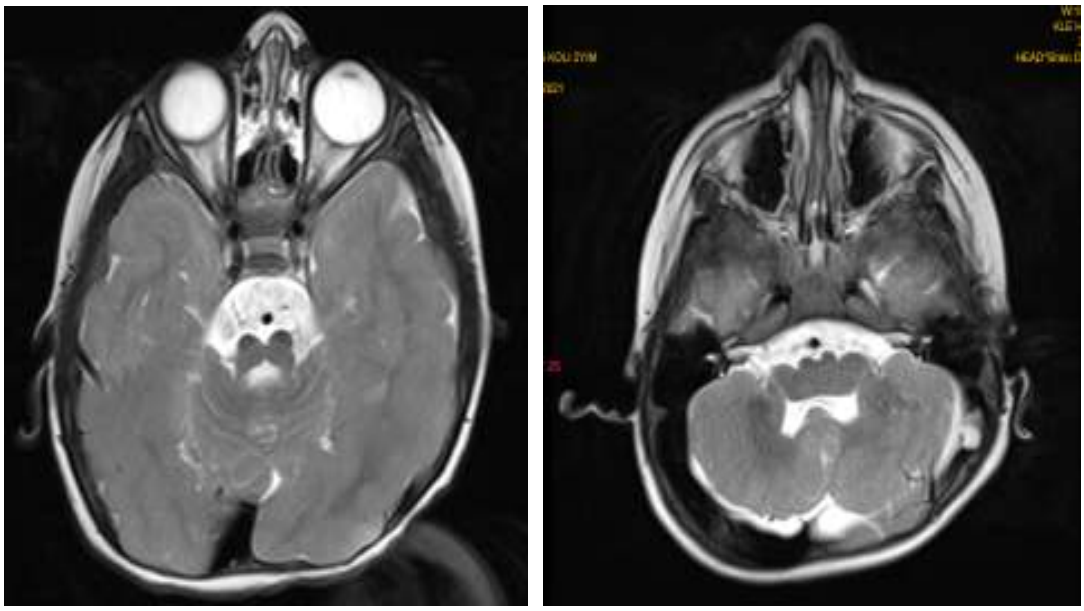


Figure 2.1 & 2.2 Axial T2 weighted images showing pontine hypoplasia

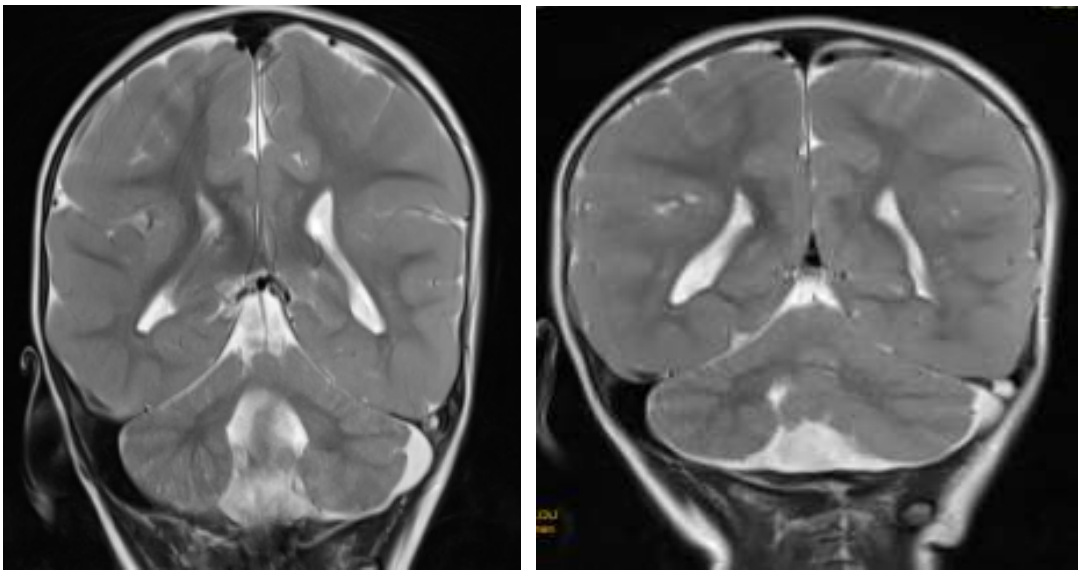


Figure 2.3 &2.4 Coronal T2 weighted images showing vermian hypoplasia

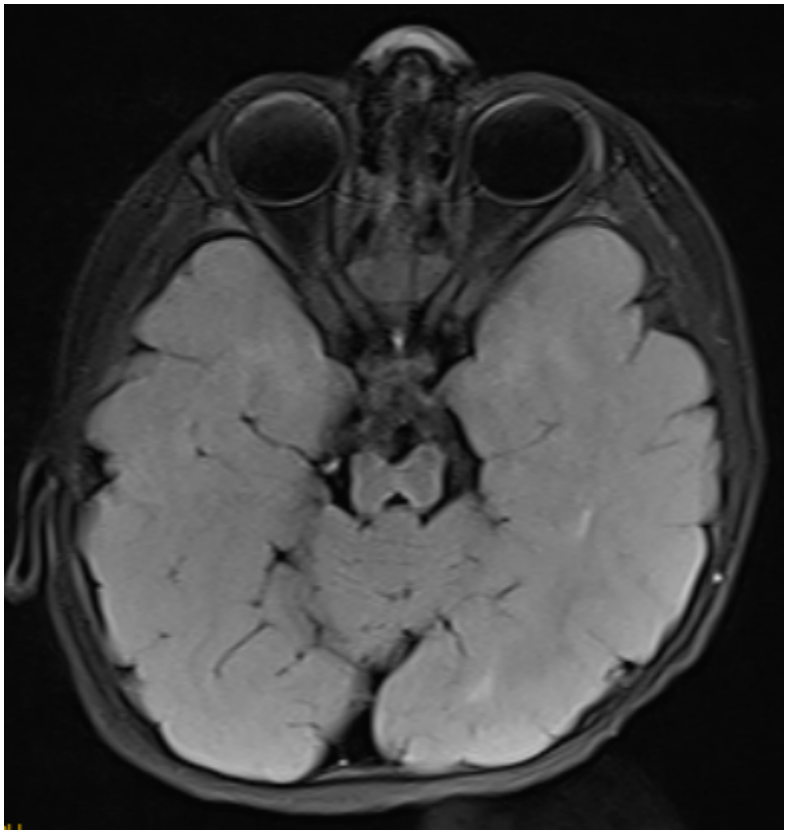
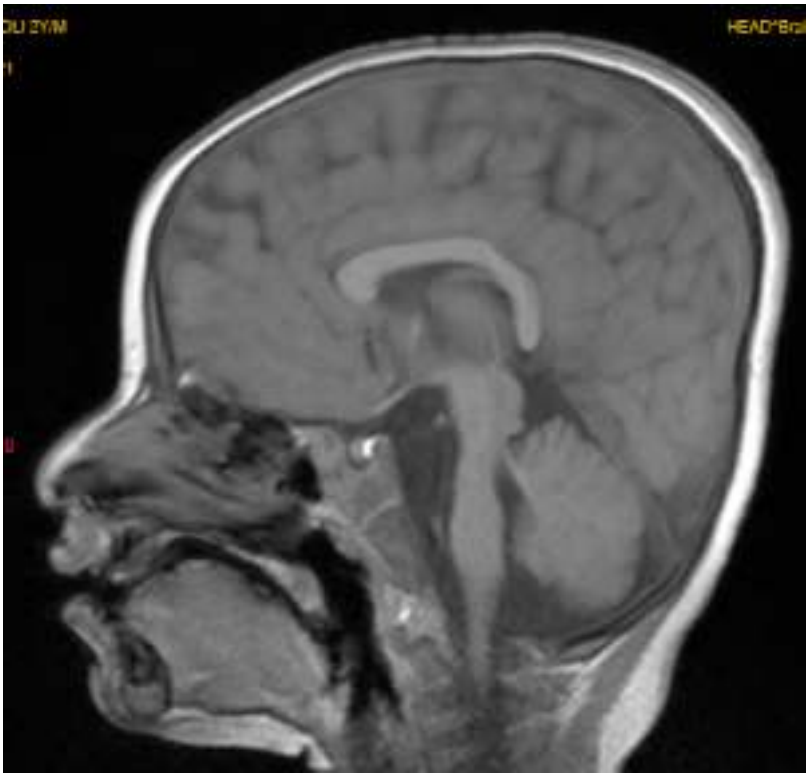


Figure 2.5AxialFLAIR images showing pontine hypoplasia with figure of 8 appearance



Fgure 2.6: Sagittal T1 weighted image showing hypoplastic brainstem

CASE 3

Another 2 year old child, who had only presented with complaints of developmetal delay was clinically suspected to have aicardia syndrome, there was seen gross cerebral asymmetry with atrophy and asymmetrical dilatation of lateral ventricles.Gross cerebral asymmetry with atrophy and asymmetrical dilatation of lateral ventricles, with polymicrogyria in left parietal region. Corpus callosaldygenesis and mild cerebellar hypolasia was also noted. Areas of blooming were noted in the left perivenrticular region which shows blooming on SWI sequence suggestive of bleed or calcification.

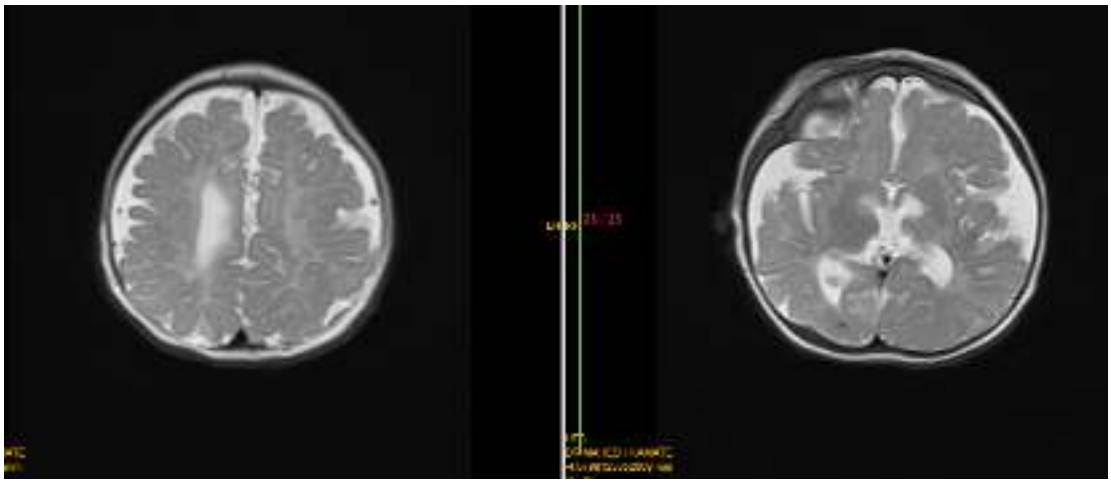


Figure 3.1 &3.2 : Axial T2 WI showing polymicrogyria in the left parietal region

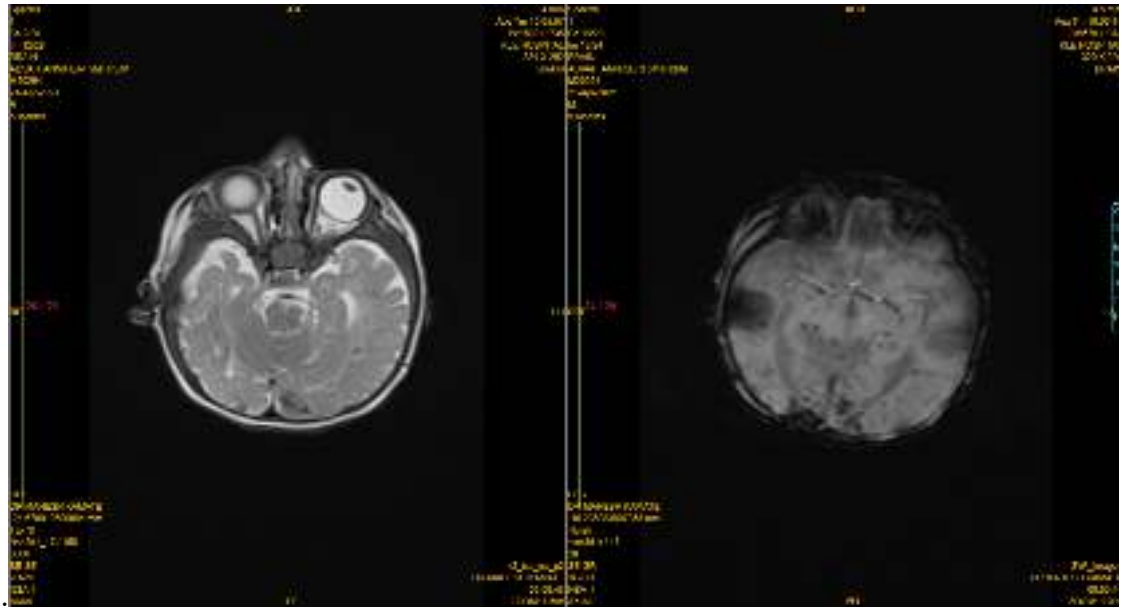


Figure 3.3 &3.4 : T2 WI and SWI axial images showing aeas of blooming in the left perivenrticular region

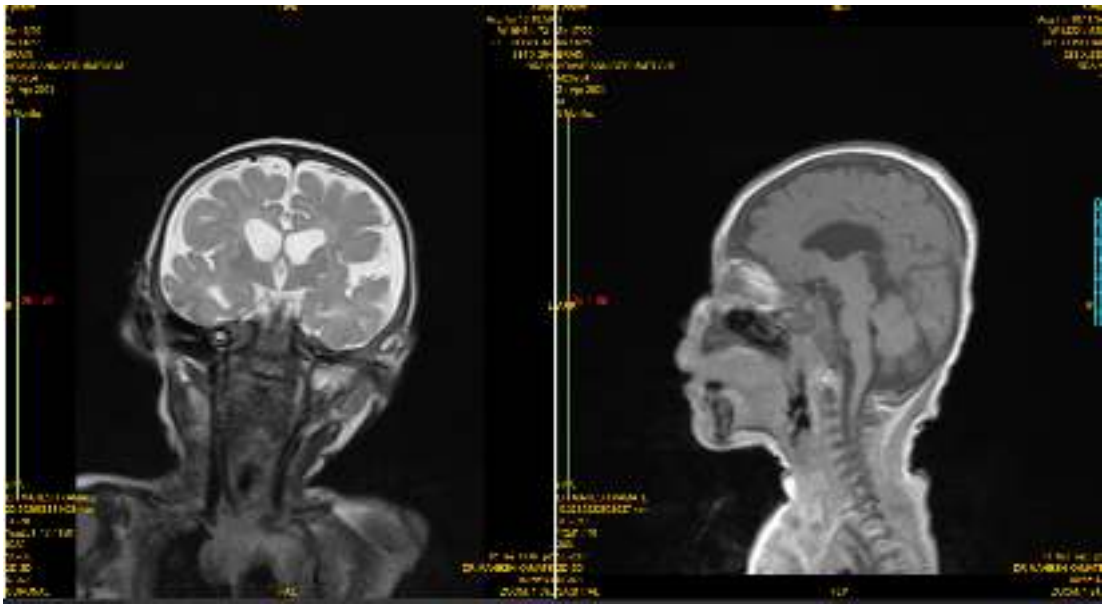


Figure 3.5 & 3.6: T2 coronal and T1 sagittal images showing corpus callosal dygenesis and mild cerebellar hypolasia

CASE 4

A 6 year old male child had complaints of developmental delay and refractory seizures .MRI brain done at the age of 1 year showed left hemi-atrophy predominantly in the fronto-parietal and temporal regions with prominence of sulci.Neuro-navigation guided corpus callosotomy was done at 4 years of age. The patient had again presented with seizure episodes. The child was clinically diagnosed as hemiplegia-hemiconvulsion epilepsy syndrome.On getting repeat MRI similar findings of left hemiatrophy with subdural hygroma in the left frontal region was noted.

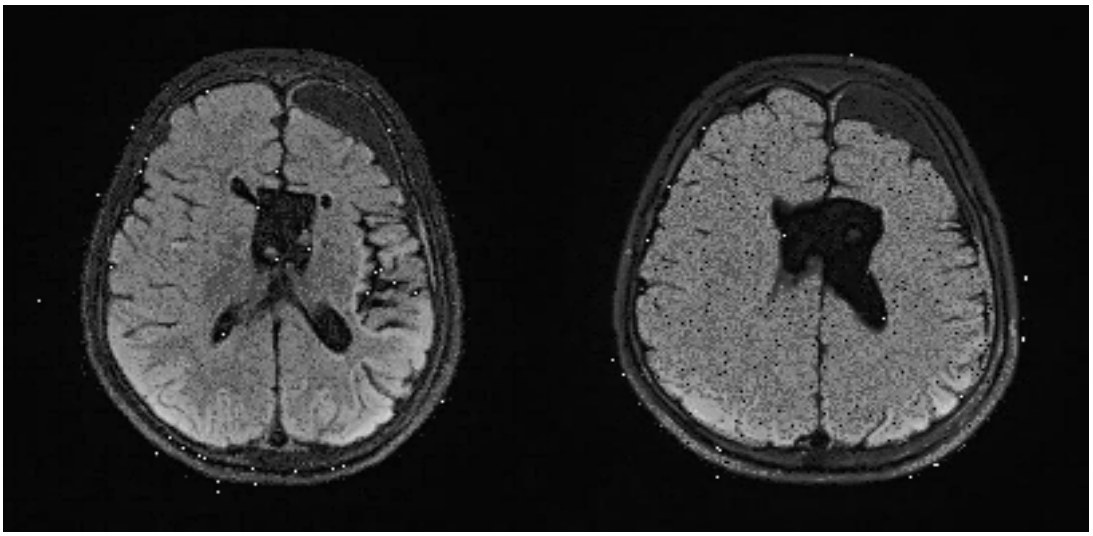


Figure 4.1 & 4.2: Axial T1 weighted images left hemi-atrophy with subdural hygroma in the left frontal region

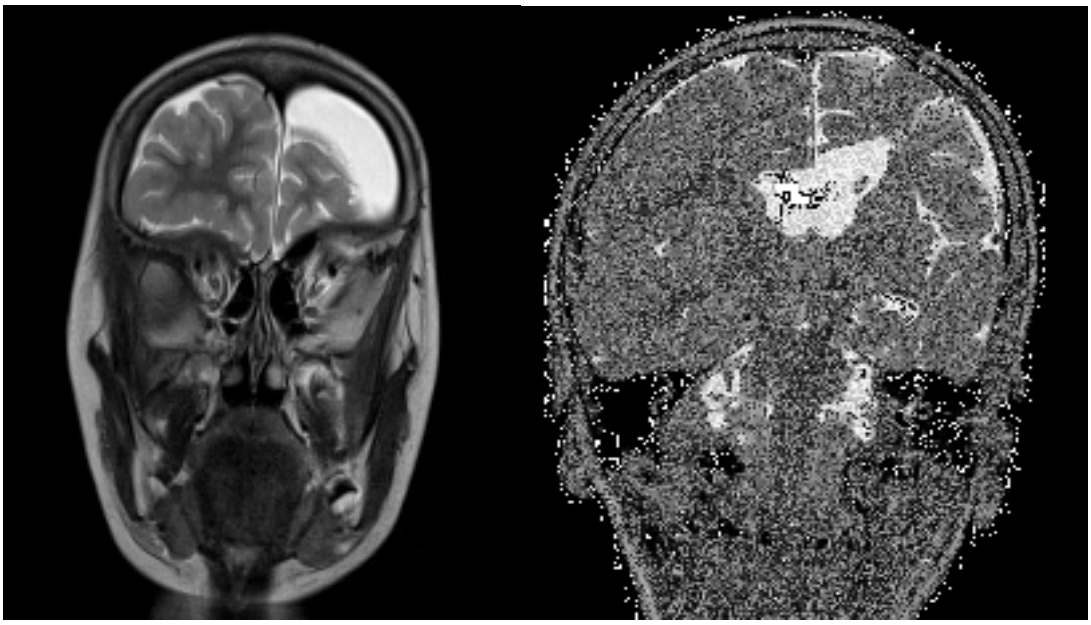


Figure 4.3 & 4.4: T2 coronal weighted image showing corpus callosotomy tract in left frontal region with subdural hygroma in left frontal region

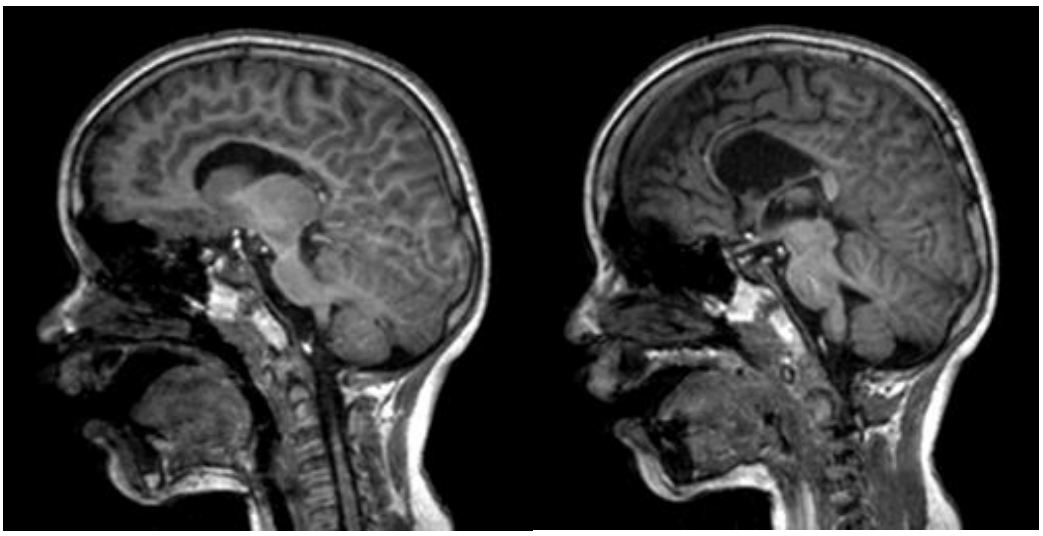


Figure 4.3 & 4.4: T1 MPRAGE sagittal images showing corpus callosotomy

CASE5

7 year old female presented with complaints of developmental delay and seizures since birth with insignificant birth history. MRI showed grey matter heterotopia with T1 and T2 isointense nodules in the bilateral lateral ventricles. Focal T1 hypointense and T2 and FLAIR hyperintense area noted in the left parietal subcortical region. The features were more in favour of tuberous sclerosis.

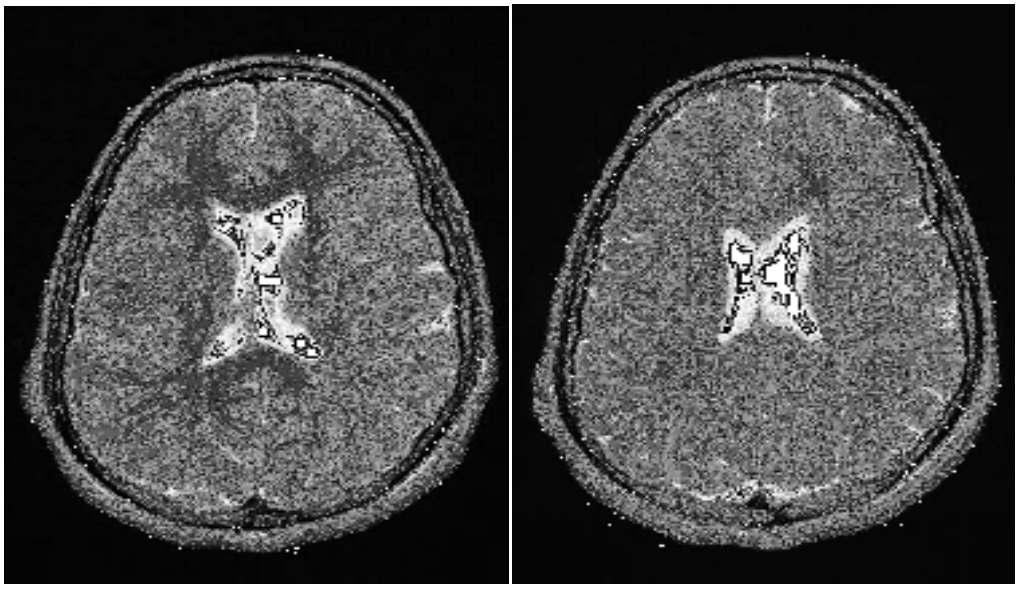


Figure 5.1 & 5.2 Axial T2 weighted images showing isointense nodule in lateral ventricle

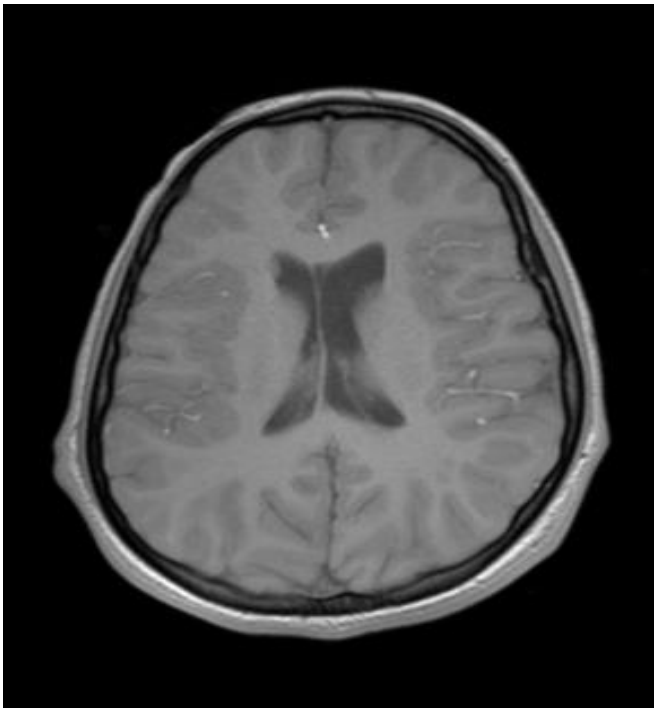


Figure 5.3: Axial T1 weighted images showing isointense nodule in right lateral ventricle

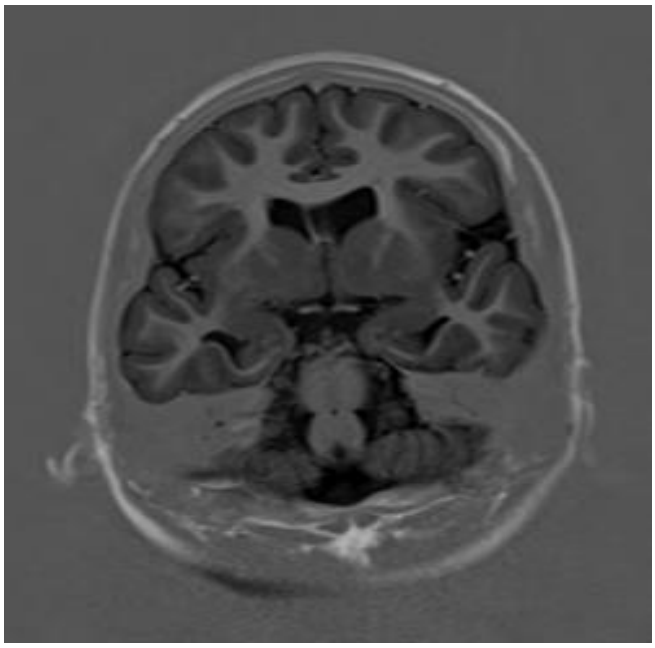


Figure 5.4: Coronal T1 weighted MPRAGE image

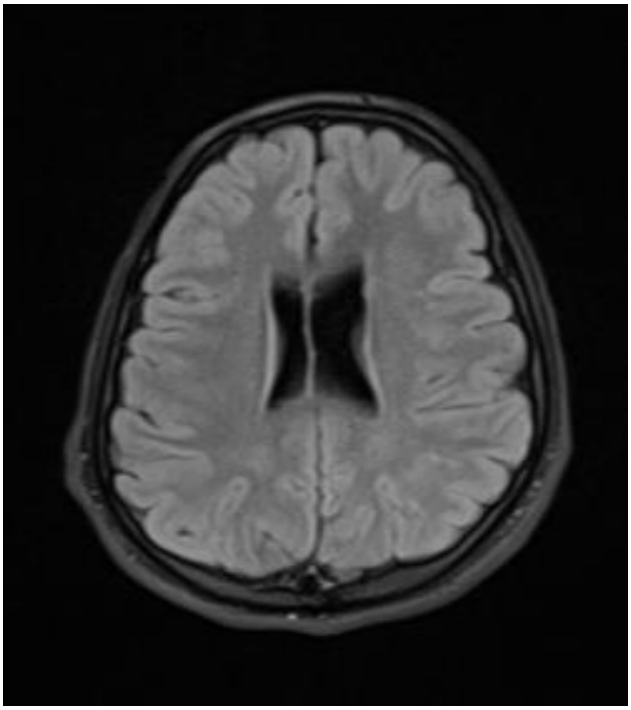


Figure 5.5 : Axial FLAIR image showing hyperintense area in left parietal region

CASE 6

6 month year old male child with complaints of right sided hemiplegia and no neck holding was found to have a space occupying lesion in the left temporal region. The lesion shows peripheral areas of restriction on DWI sequence and blooming on SWI sequence. The lesion shows mass effect on the adjacent brain parenchyma, midbrain and left temporal horn lateral ventricle. There is seen compression on the supra linoid portion of left internal carotid artery and M1 segment of left MCA.

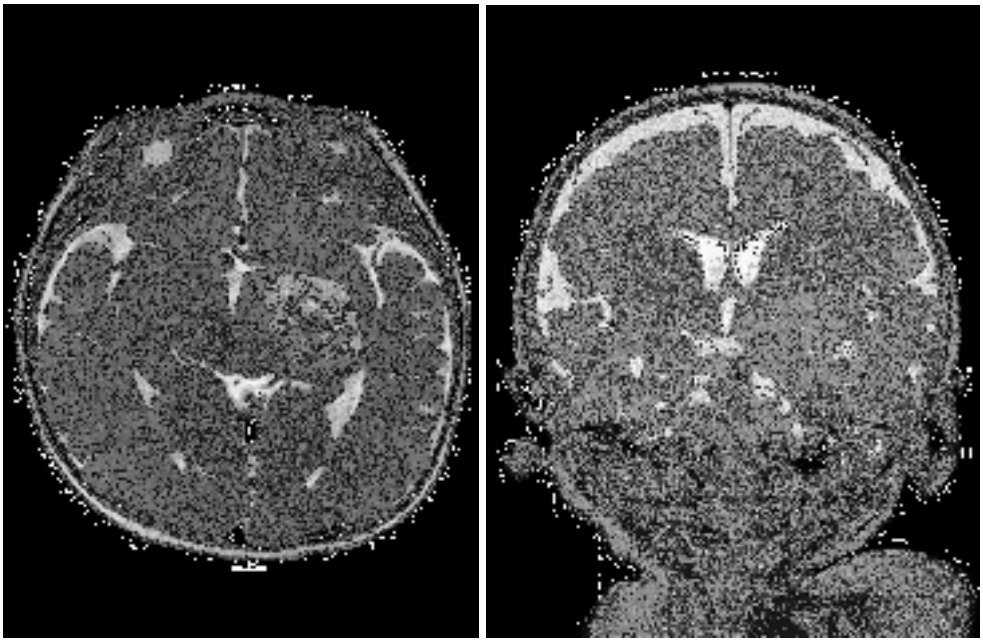


Figure 6.1 &6.2 :Axial and coronal image showing space occupying lesion in left temporal region

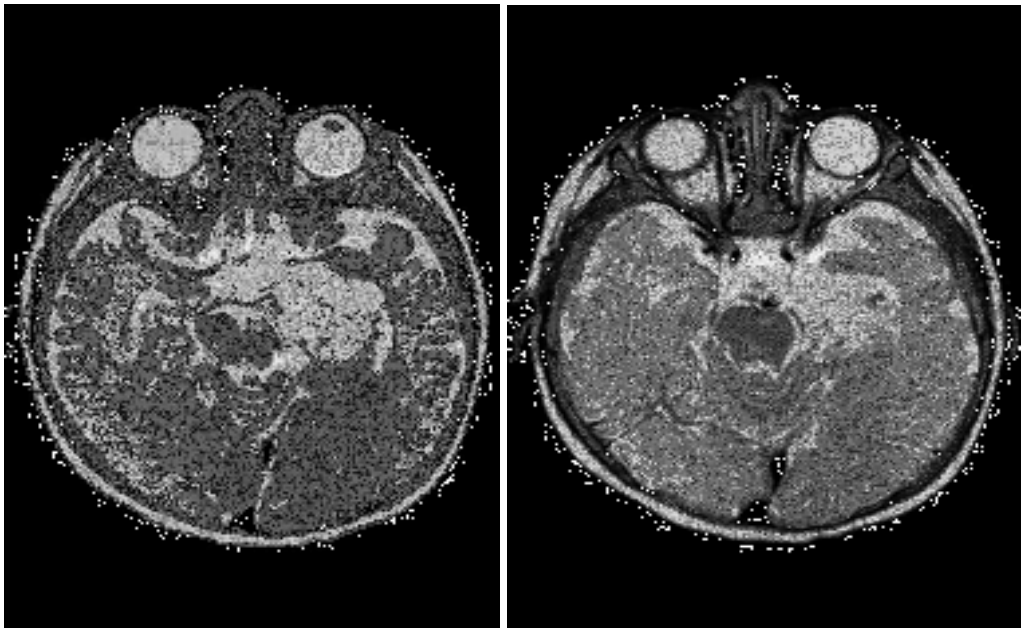


Figure 6.3 &6.4 :Axial T2 weighted image showing space occupying lesion in left temporal region

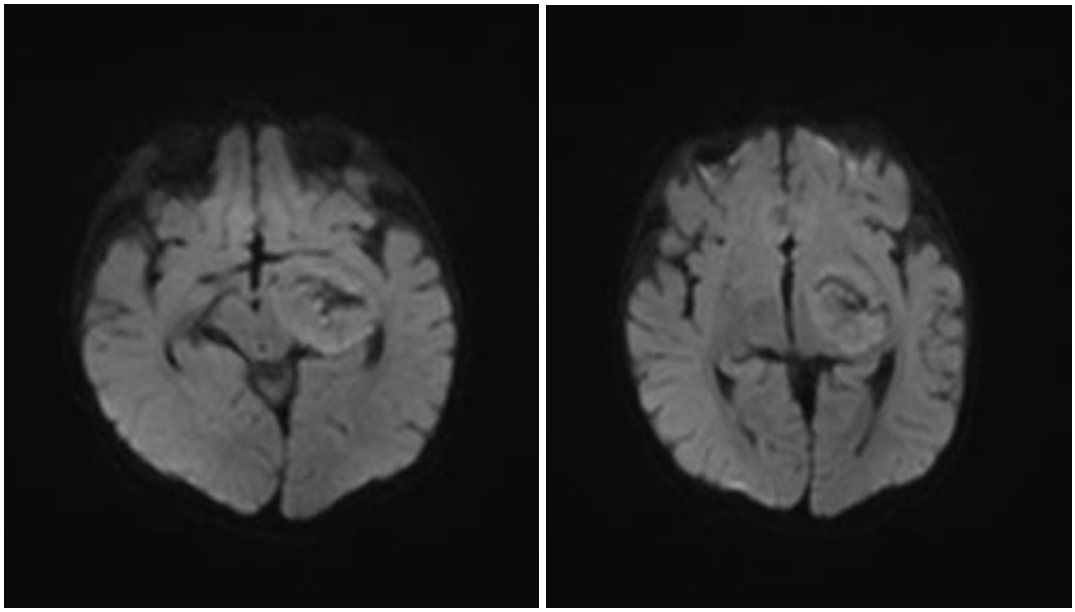


Figure 6.5 &6.6 :Axial Susceptibility weighted image showing space occupying lesion in left temporal region

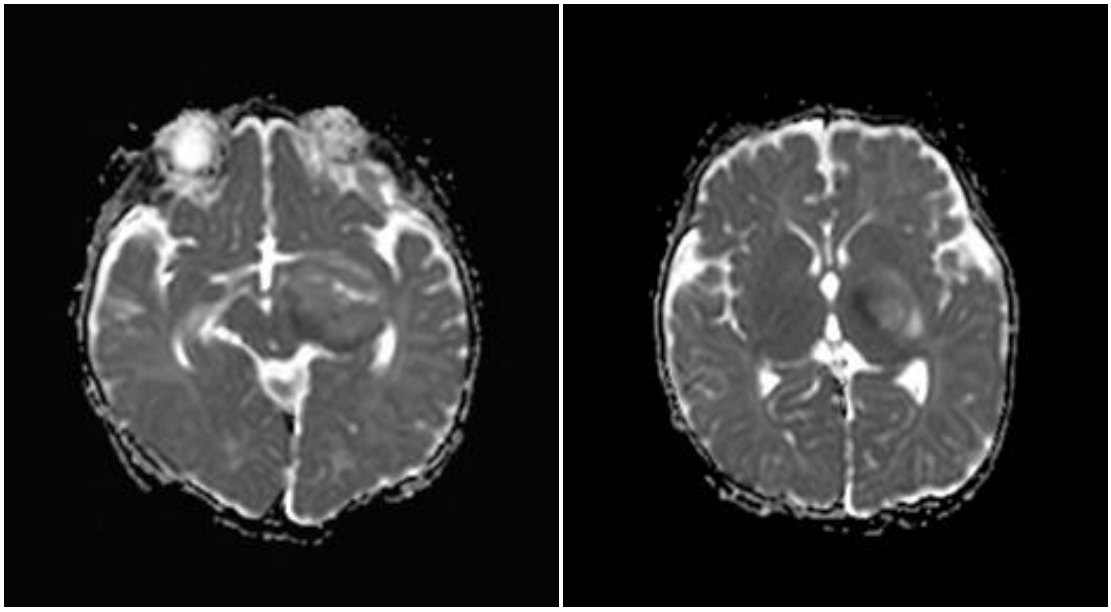


Figure 6.7 &6.8 :Axial ADC image showing space occupying lesion in left temporal region

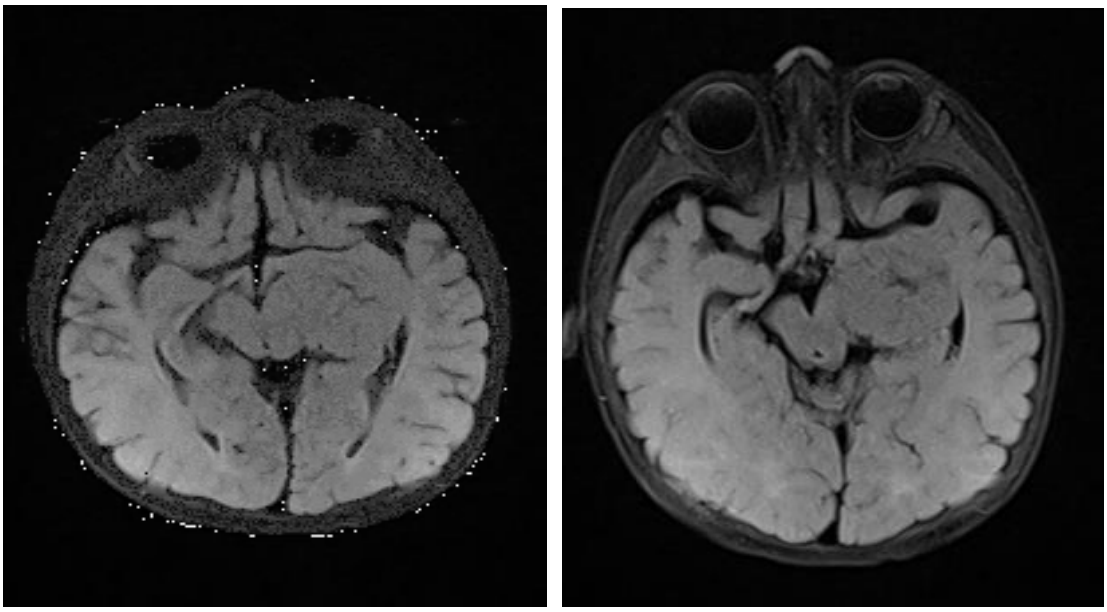


Figure 6.9 &6.10 :Axial flair image showing space occupying lesion in left temporal region

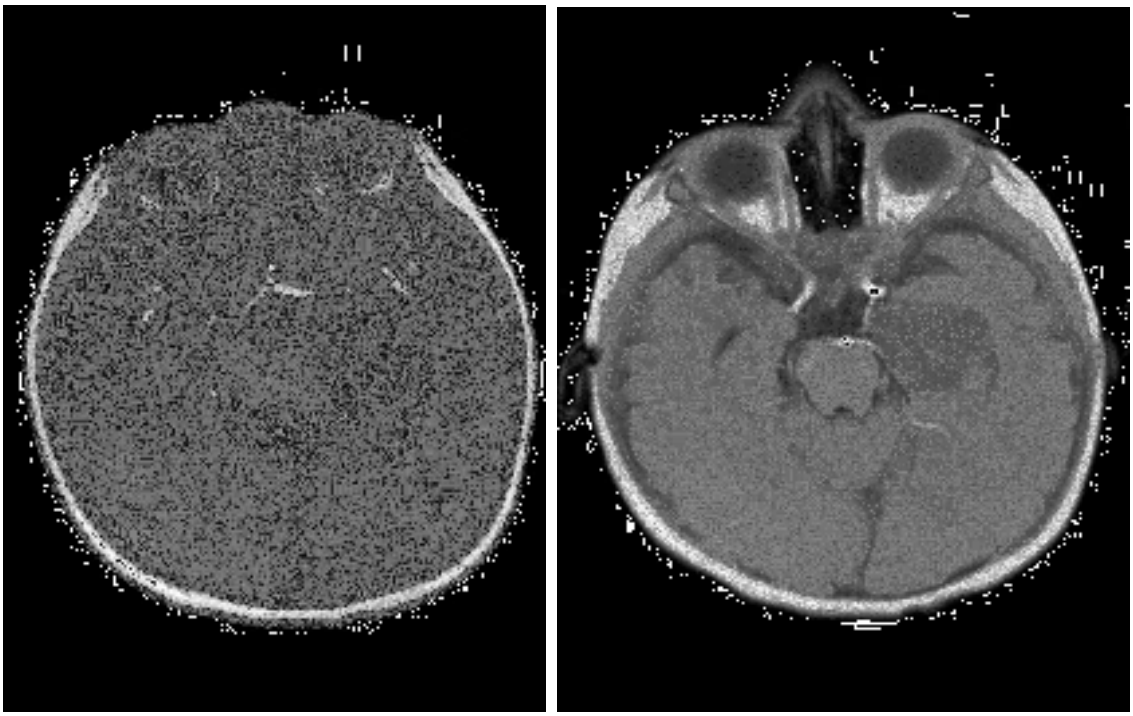


Figure 6.11 &6.12 :Axial T1 image showing space occupying lesion in left temporal region

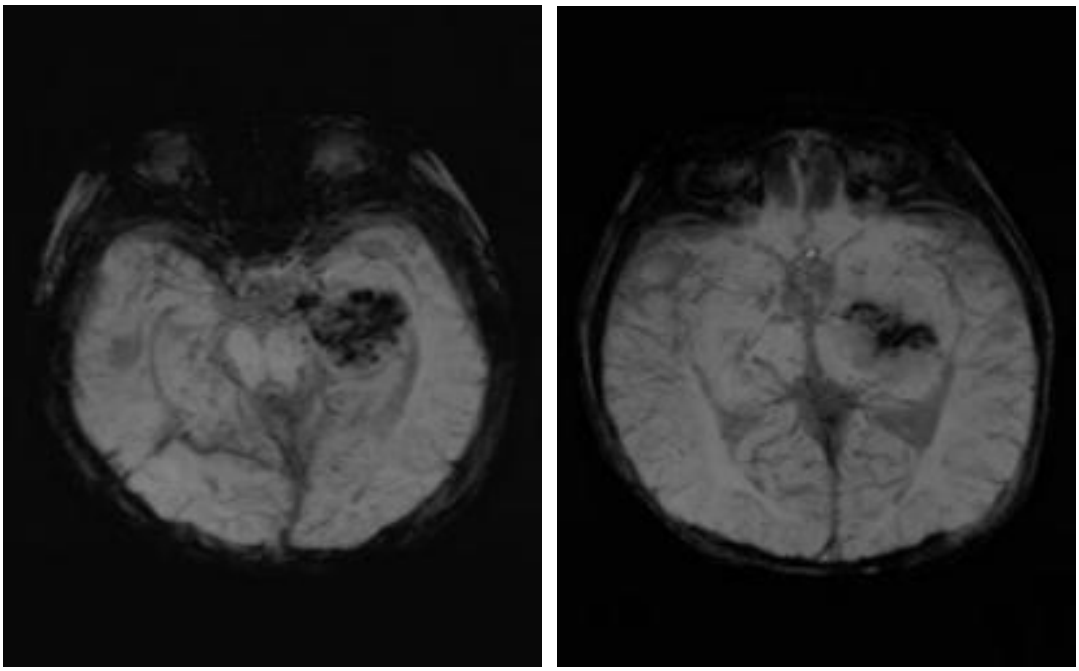


Figure 6.13 &6.14 :Axial SWI image showing space occupying lesion in left temporal region

CASE 7 :

3 month old female born out of consanguineous marriage and with insignificant birth history, presented with absent neck holding. MRI done showed non visualization of corpus callosum with non visualization of the frontal horns suggestive agenesis of corpus callous. A peri-callosallipoma with calcifications was noted. Colpocephaly was also noted.

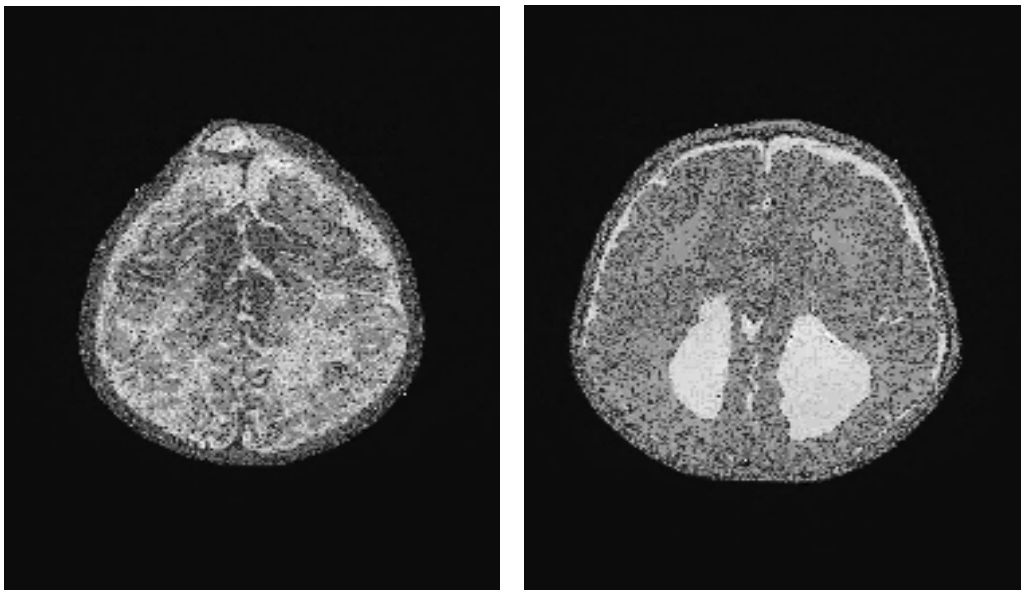


Figure 7.1 & 7.2 :Axial T2 image showing peri-callosallipoma and well defined subcutaneous lesion in frontal region

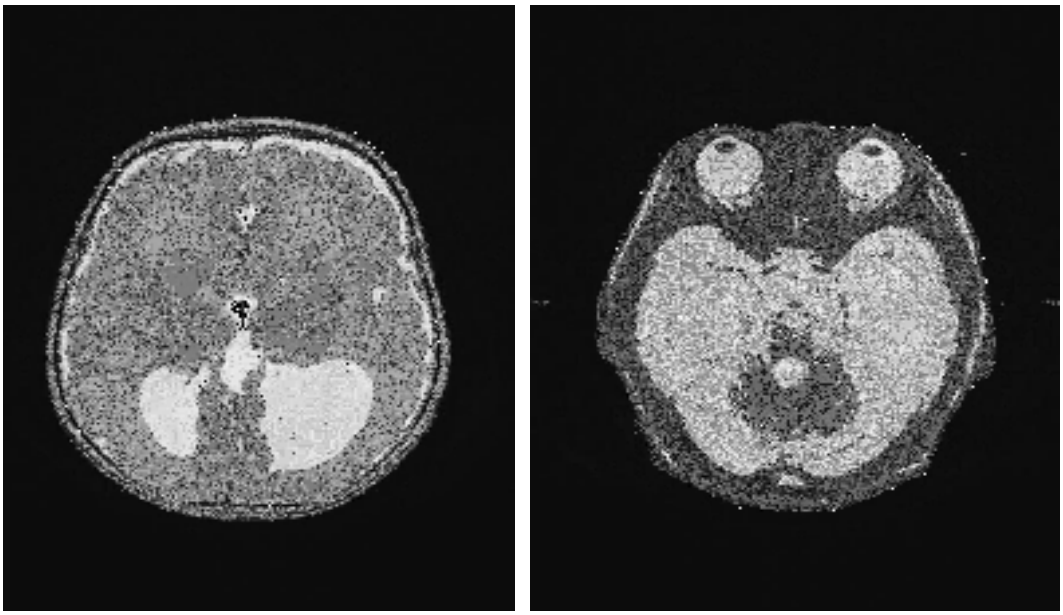


Figure 7.3 & 7.4 :Axial T2 image showing colpocephaly

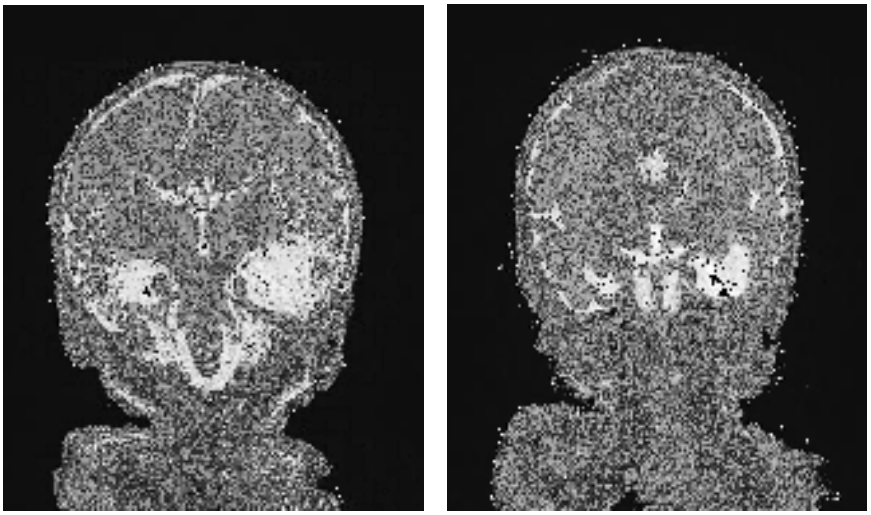


Figure 7.5 & 7.6 :Coronal T2 image showing peri-callosallipoma with non visualization of the frontal horn of lateral ventricles.

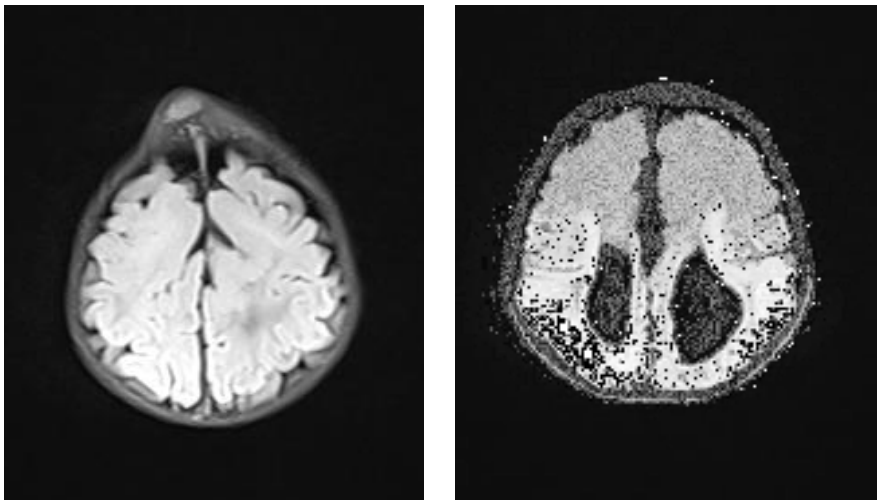


Figure 7.7 & 7.8 :Axial FLAIR image showing peri-callosal lipoma with non visualization of the frontal horn of lateral ventricles.

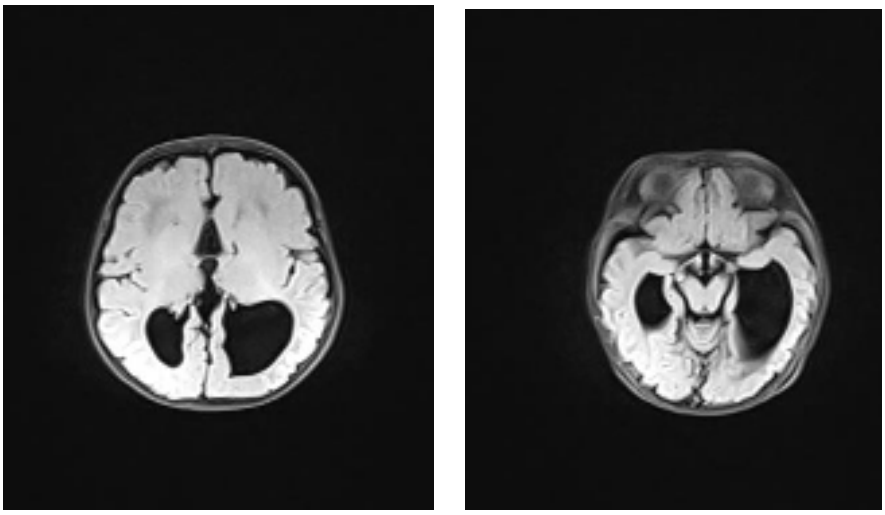


Figure 7.9 & 7.10 :Axial FLAIR image showing colpocephaly

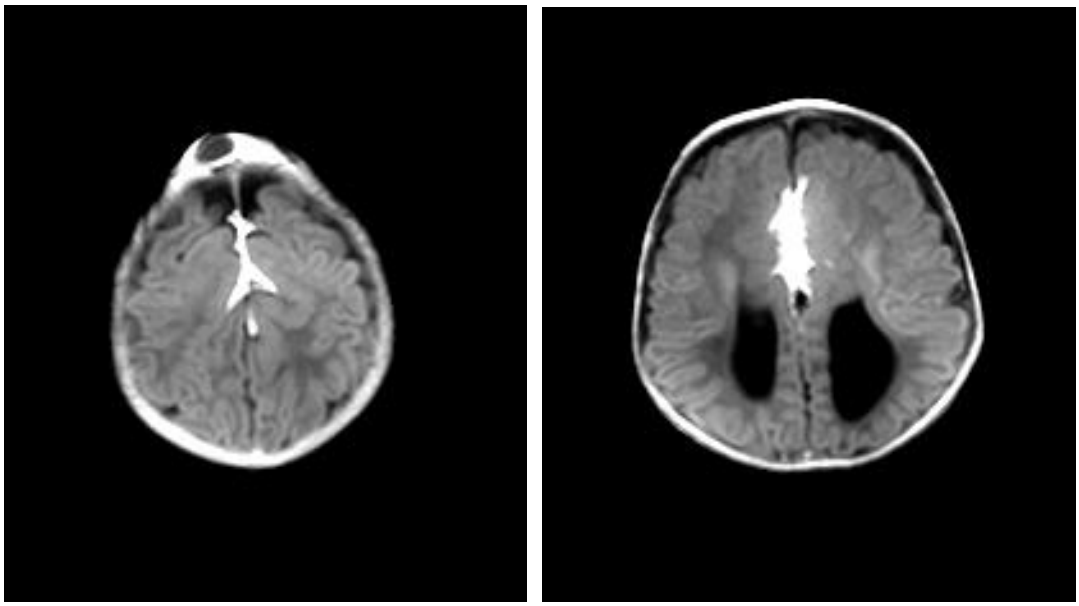


Figure 7.11 & 7.12 :Axial T1 image showing peri-callosallipoma with non visualization of the frontal horn of lateral ventricles.

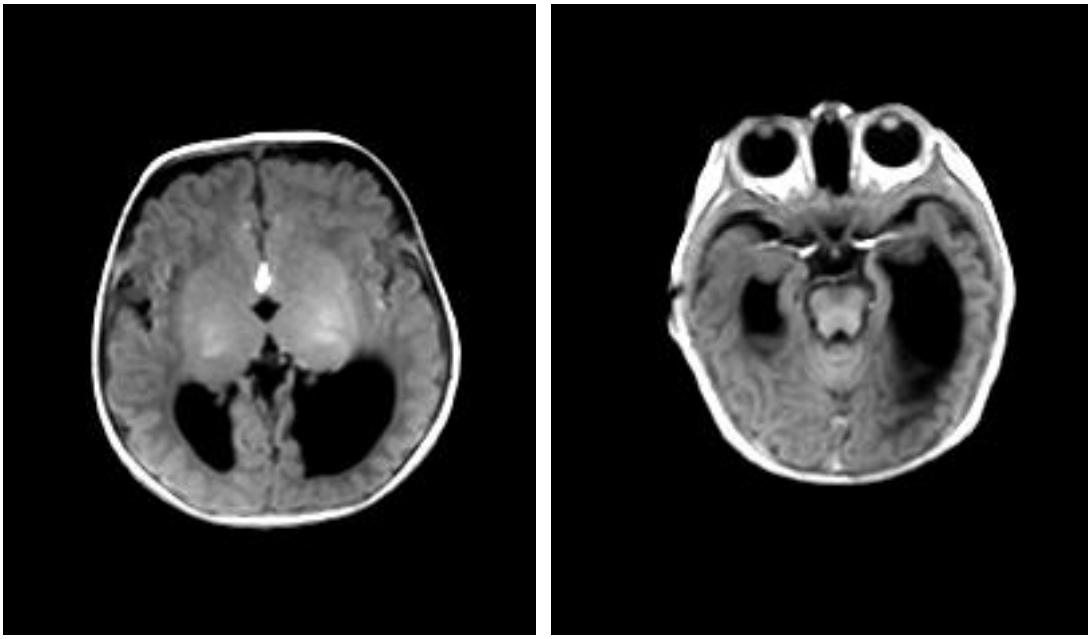


Figure 7.13 & 7.14 :Axial FLAIR image showing colpocephaly

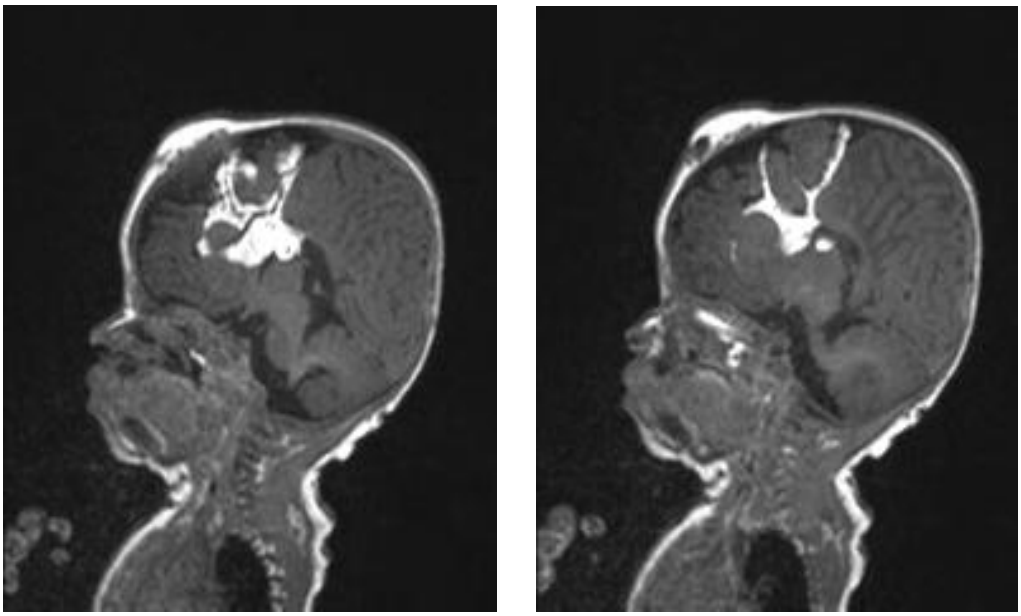


Figure 7.15 & 7.16 :Sagittal T1 weighted images showing T1 hyperintense lipoma along the interhemispheric fissure

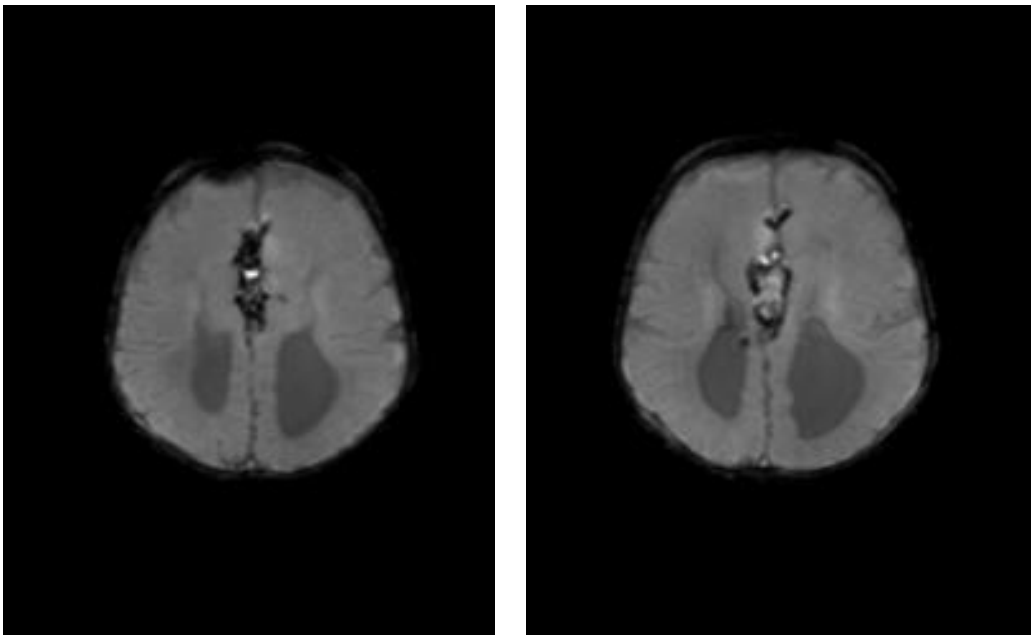


Figure 7.17 7.1 : Axial SWI sequence showed areas of blooming suggestive of calcifications

CASE 8:

A 7yr old male , born out of non consanguineous marriage, with normal vaginal delivery, was born preterm, cried immediately after birth and had no history of hypoxic insult or NICU admission . On MRI images , there was seen a cleft in the left parietal region lined by grey matter. There was seen thickening of sulci in the left fronto-parietal region suggestive of lizzencephaly-pachygyria spectrum, mild prominence of right lateral ventricle noted. Focal gliotic area was also noted in the right cerebellar region.diffuse mild thiining of corpus callosum noted.

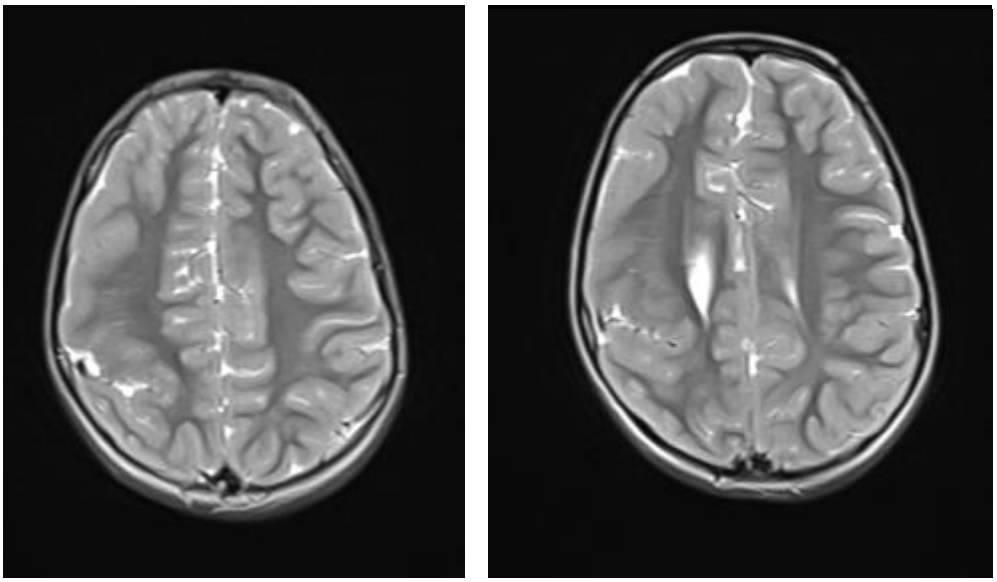


Figure 8.1 &8.2 : Axial T2 weighted images a cleft in the left parietal region lined by grey matter

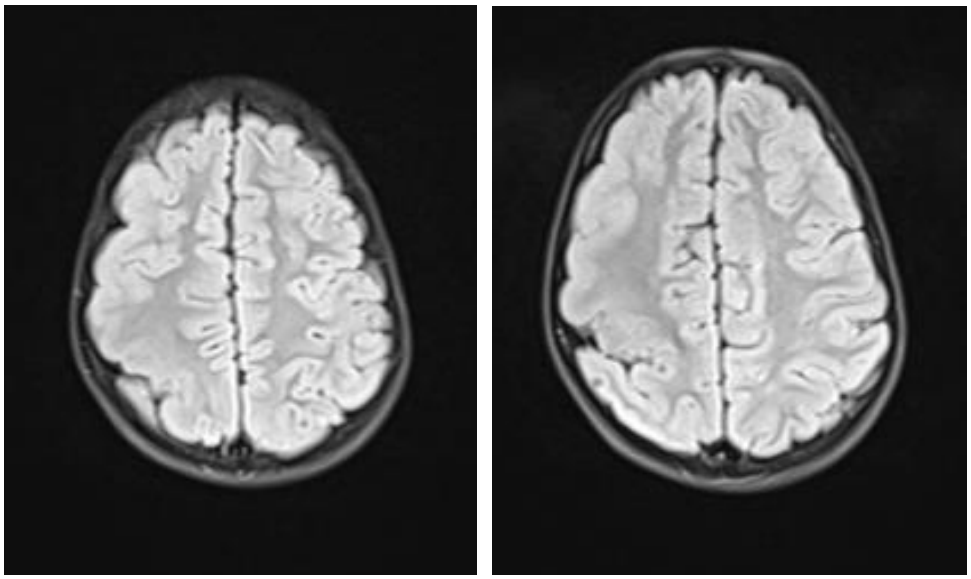


Figure 8.3 &8.4 : Axial T2 weighted images a cleft in the left parietal region lined by grey matter

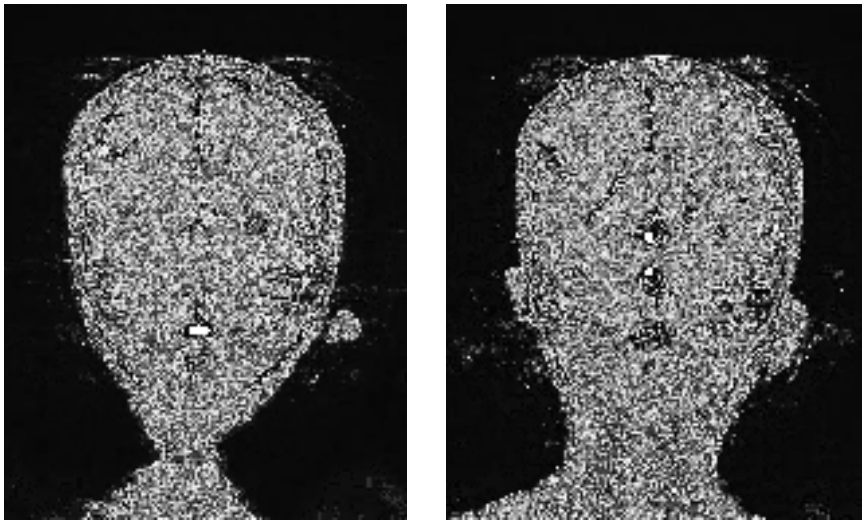


Figure 8.5 &8.6 : Coronal T2 weighted images showing thickening of sulci in the left fronto-parietal region

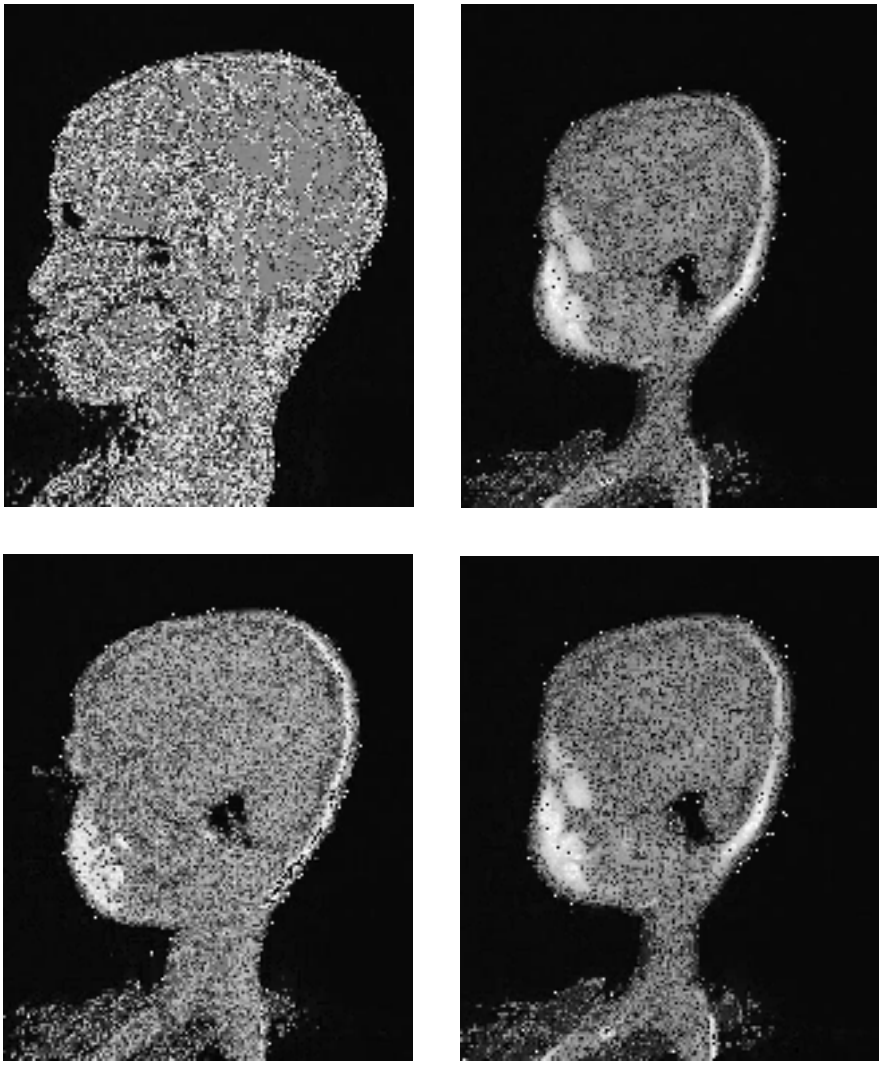


Figure 8.7, 8.8, 8.9 & 8.10 : Sagittal T1 weighted images shoing cleft in the left parietal region

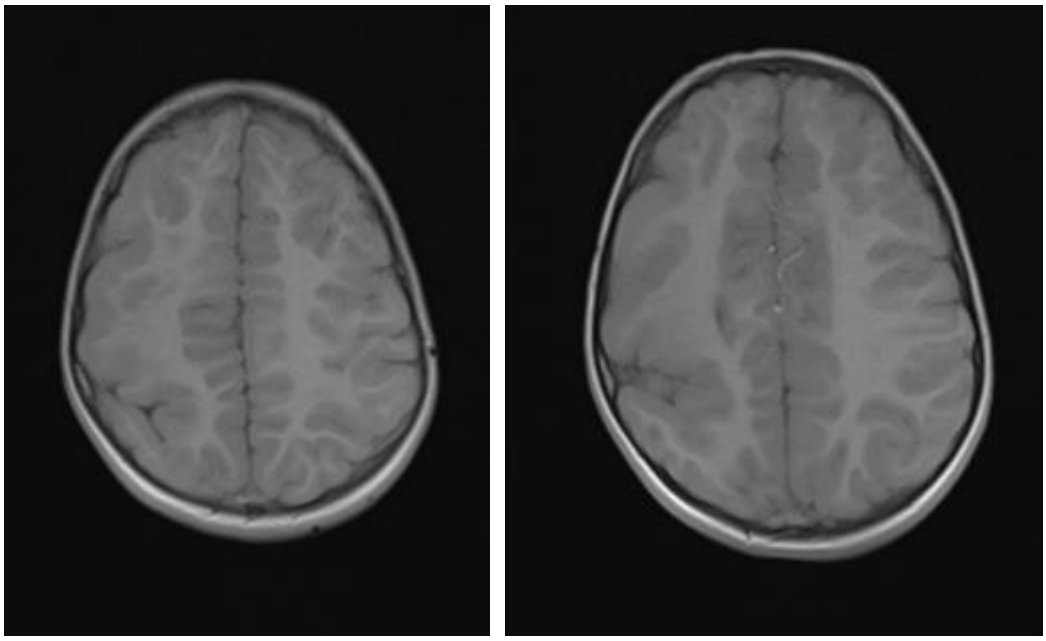
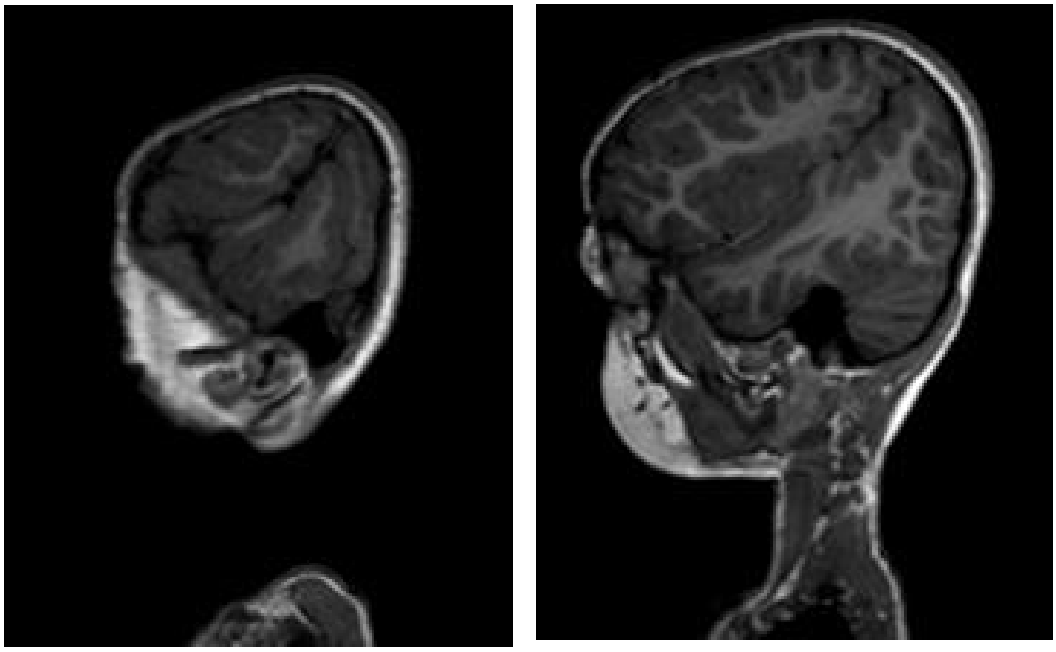


Figure 8.11 &8.12 : T1 weighted axial images



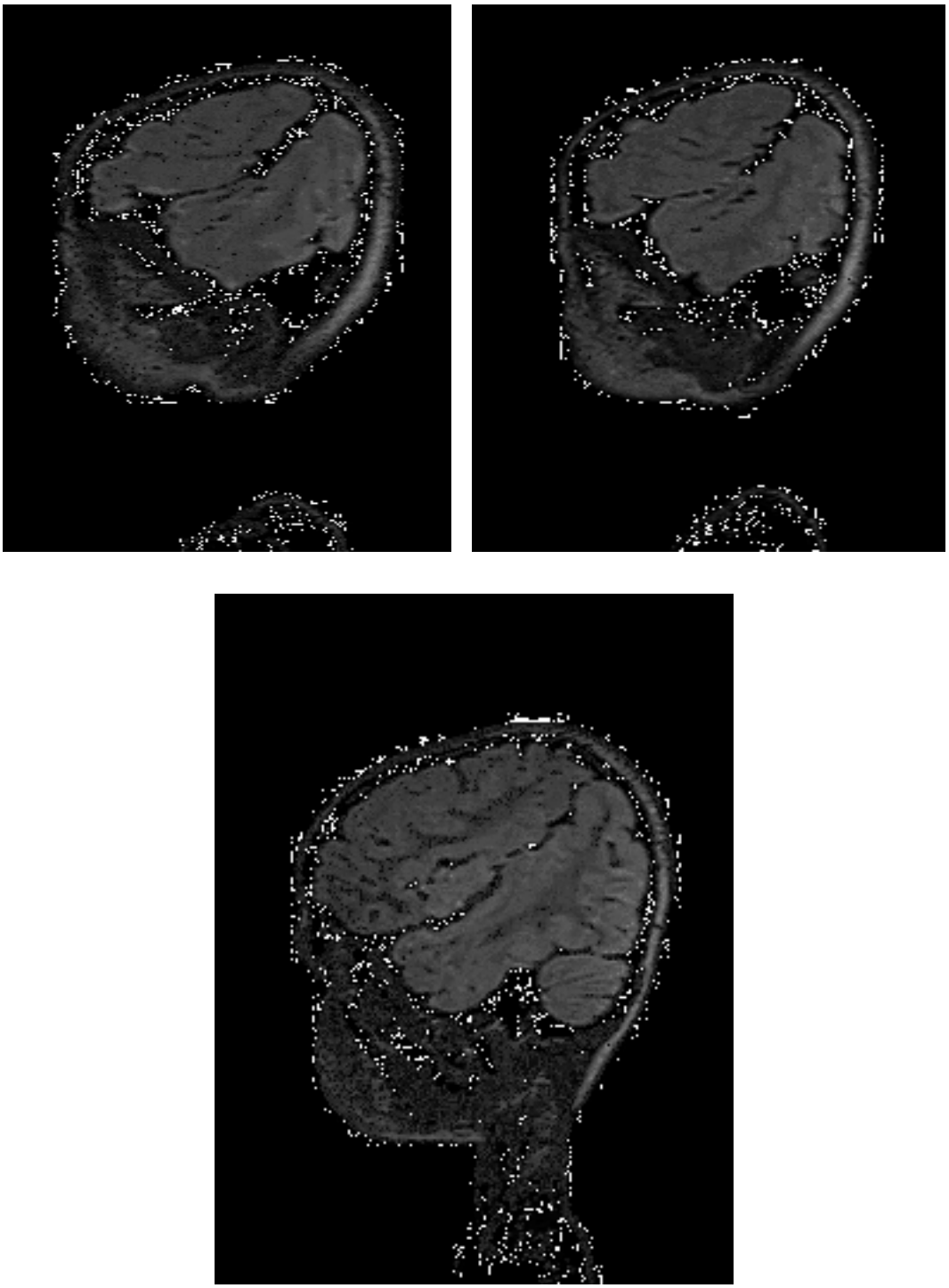


Figure 8.13, 8.14, 8.15 , 8.16 and 8.17 : Sagittal MPRAGE images showing cleft in the left parietal region

CASE 9 :

10 year old female, presented with complaints of global developmental delay, drooling of saliva, feeding and speech difficultyand severe intellectual disability. The child was second born to second degree consanguineous marriage. The child had a full term normal vaginal delivery, however has weak cry at birth with NICU stay for 3days. On examination the child had microcephaly, sever intellectual disability and quadriparesis was noted.MRI done showed non specific changes in bilateral peritrigonal, periventricular region and fronto-parieto-temporal subcortical white matter and cerebral and cerebellar atrophy. T1 hyperintense& T2 mixed intensity area was noted in the superior aspect of cerebellar vermis, approximately measuring 1.0 (AP) x 0.7 (ML) x 0.7 (CC) cms, and shows few areas of blooming on SWI sequence.On few cuts of CT, the lesion shows fat attenuation (Avg HU -80 to -100)….likely to be ?intracranial teratoma/dermoid/ lipoma. Clinically the child was suspected to have worster drought syndrome.

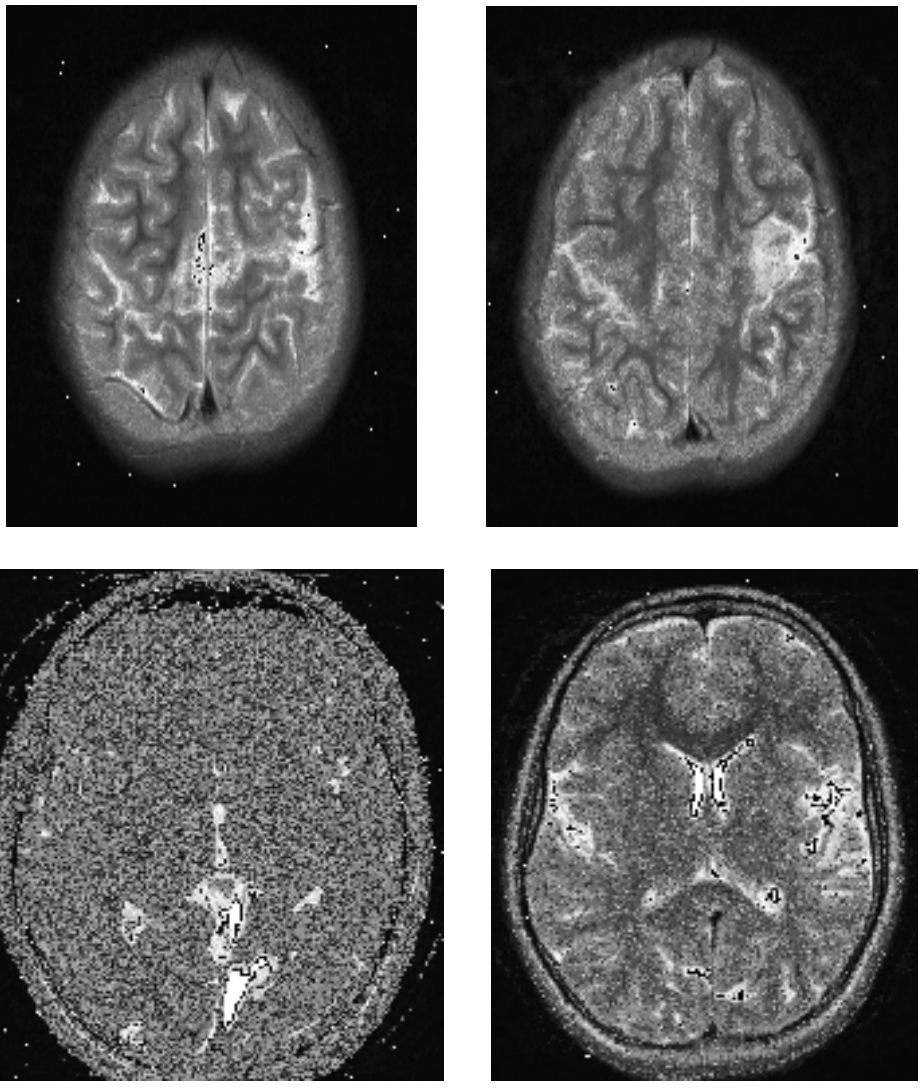


Fig 9.1, 9.2, 9.3 &9.4 : Axial T2 weighted images

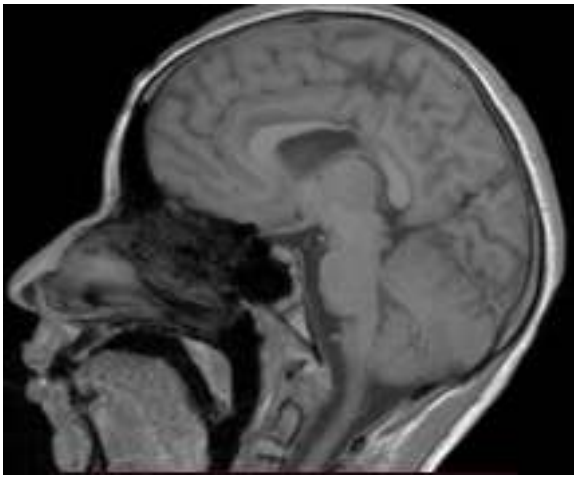
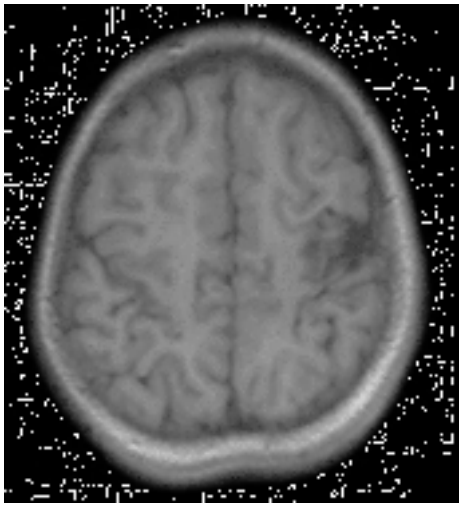


Figure 9.5 : T1 weighted sagittal image



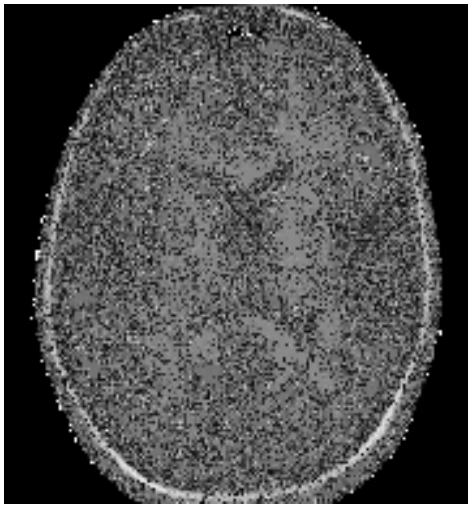
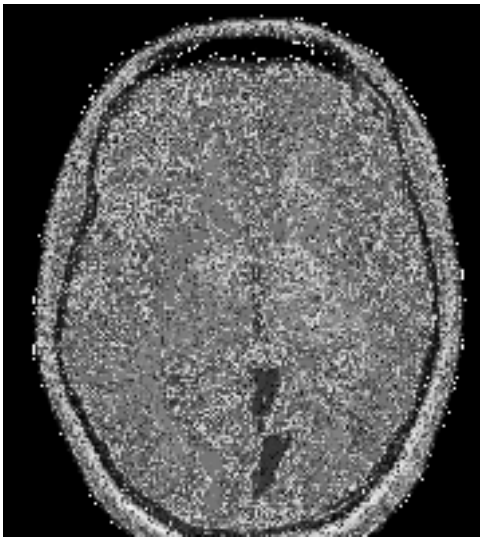


Figure 9.6 &9.7 : T1 weighted axial images



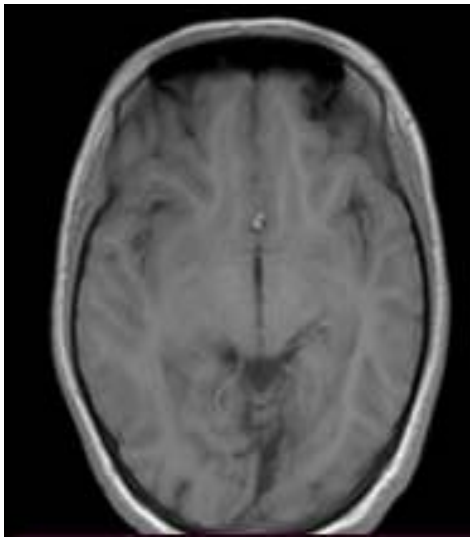


Figure 9.8 &9.9 : T1 weighted axial images

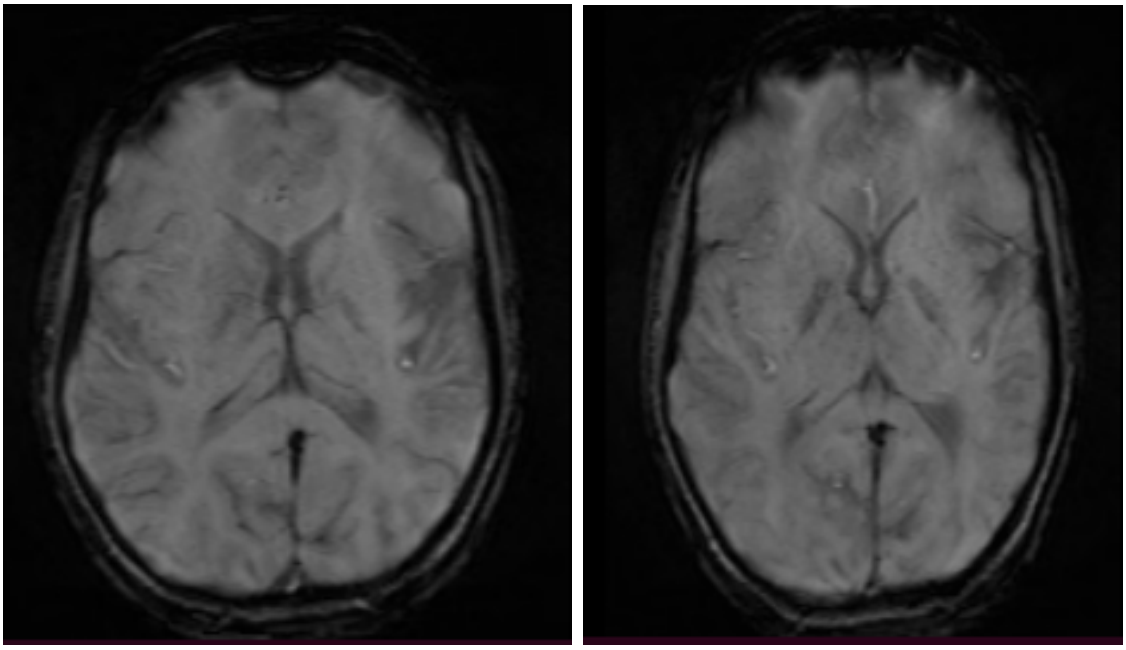


Figure 9.10 & 9.11: Axial SWI IMAGES

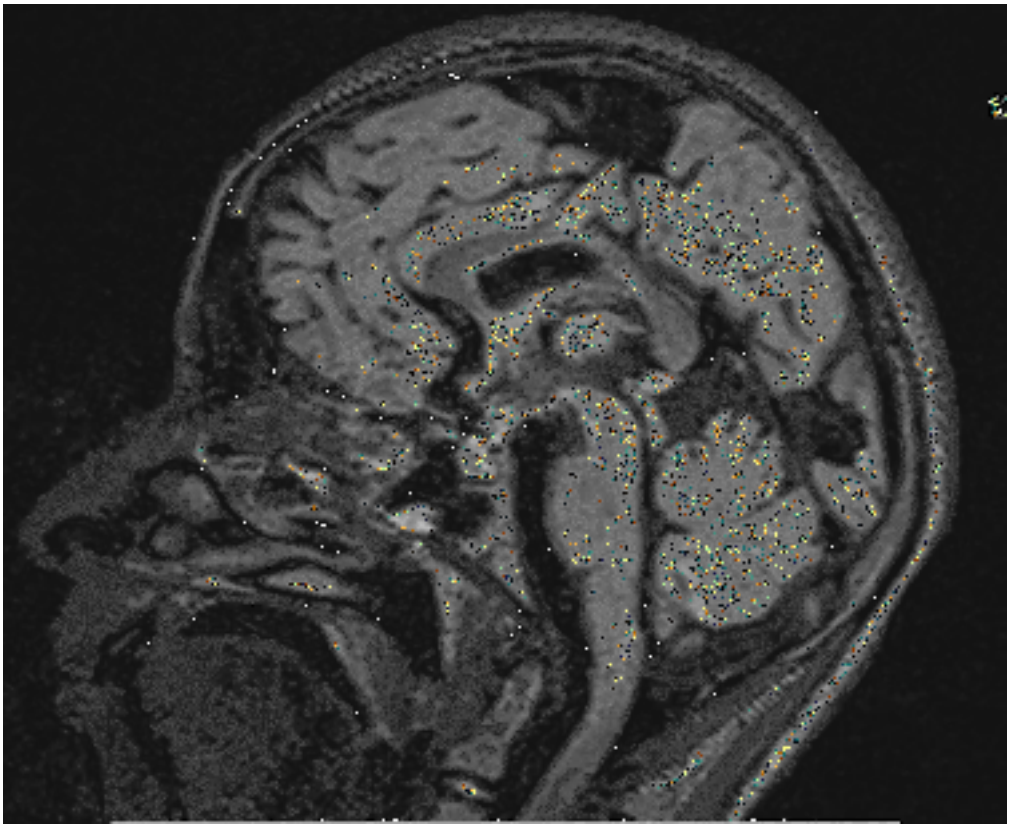


Figure 9.12 : SAGITTAL T1 MPRAGE SEQUENCE

CASE 10:

10 month old child presented with complaints of delayed milestones and irritability. The other had history of pv bleed for 3 hours before delivery. The child had full term normal vaginal delivery but did not cry immediately after birth with Type II HIE and NICU admission for 15 days. The child also had seizures on D1 of life. The child was product of 3rd degree CM. On examination child has dystonia. Mri showed T1 hyperintensities and T2 hypointensities in bilateral thalamus and putamen with no evidence of diffusion restriction on DWI sequence.There was mild dilatation of the bilateral lateral ventricle and 3rd ventricle. Atria of right lateral ventricle measures 1.2 cm. Atria of left lateral ventricle measures 1.0 cm. 3rd ventricle measures 1.2 cm. 4th ventricle measures 0.8 cm.

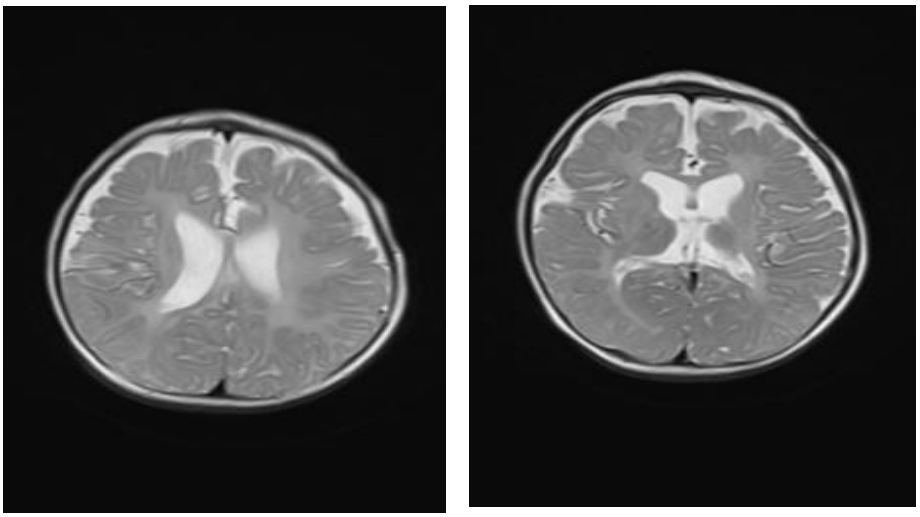


Figure 10.1 &10.2 : Axial T2 weighted images

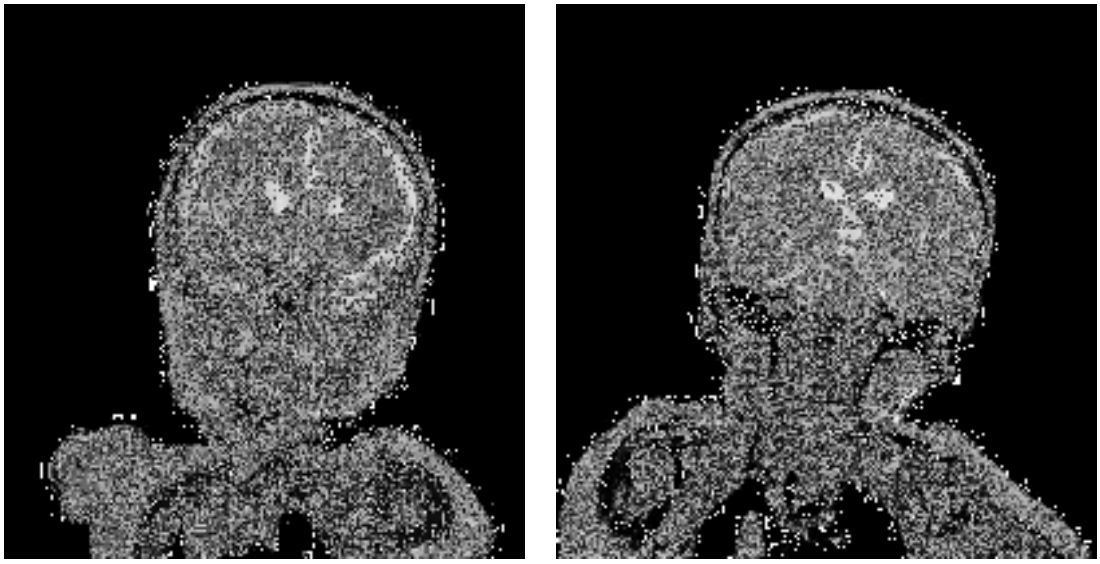


Figure 10.3 &10.4 : T2 WEIGHTED CORONAL IMAGES

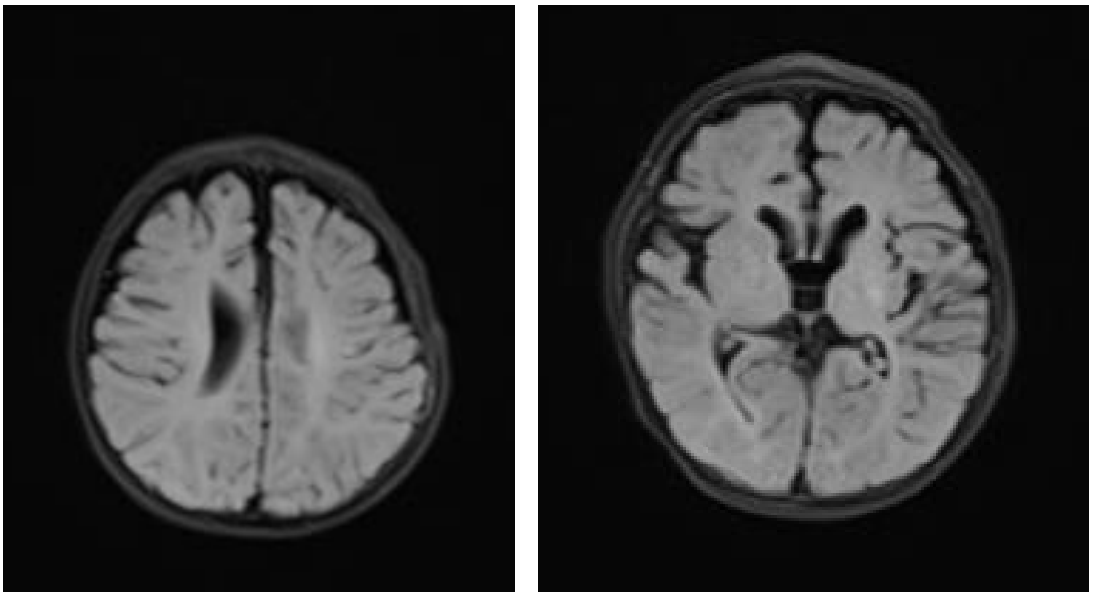


Figure 10.5 &10.6 T1 WEIGHTED AXIAL IMAGES

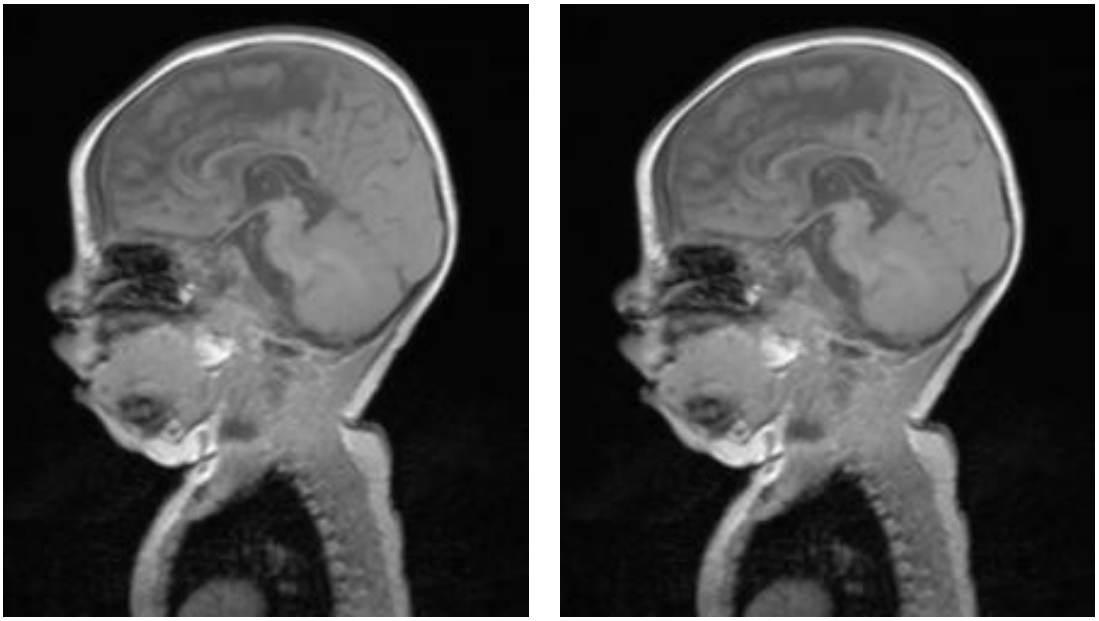


Figure 10.7 &10.8 :T1 SAGITTALIMAGES

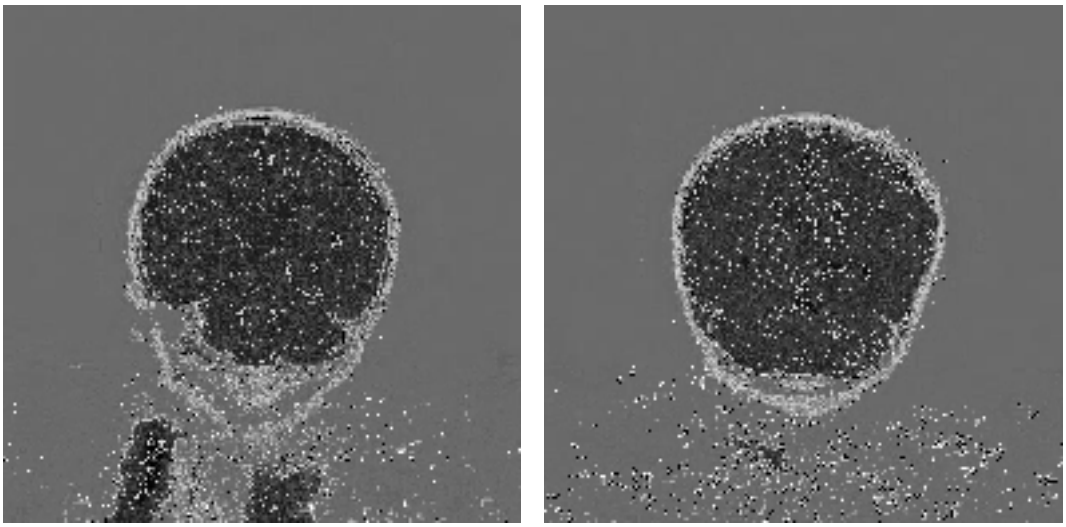


Figure 10.9, 10.10 & 10.11: Sagittal and coronal MPRAGE images

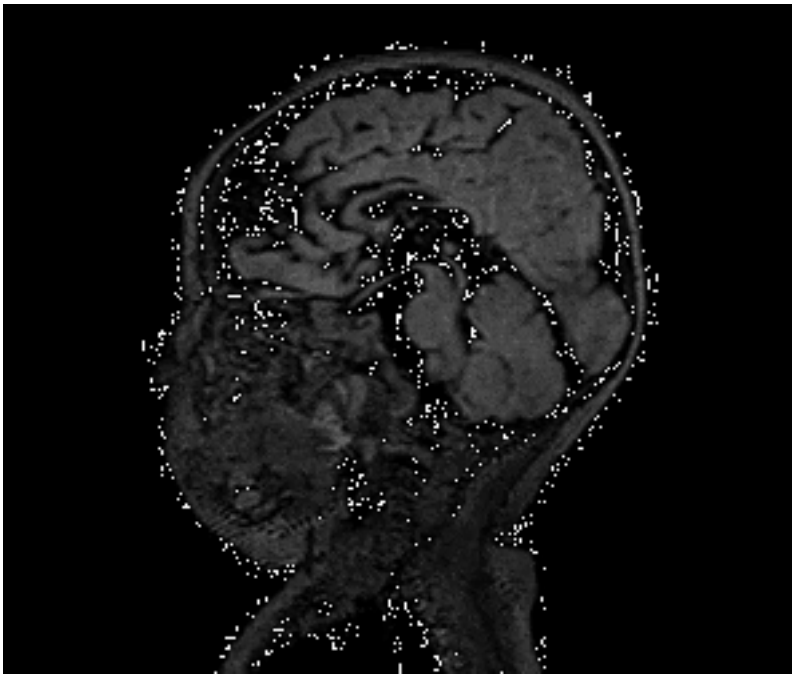
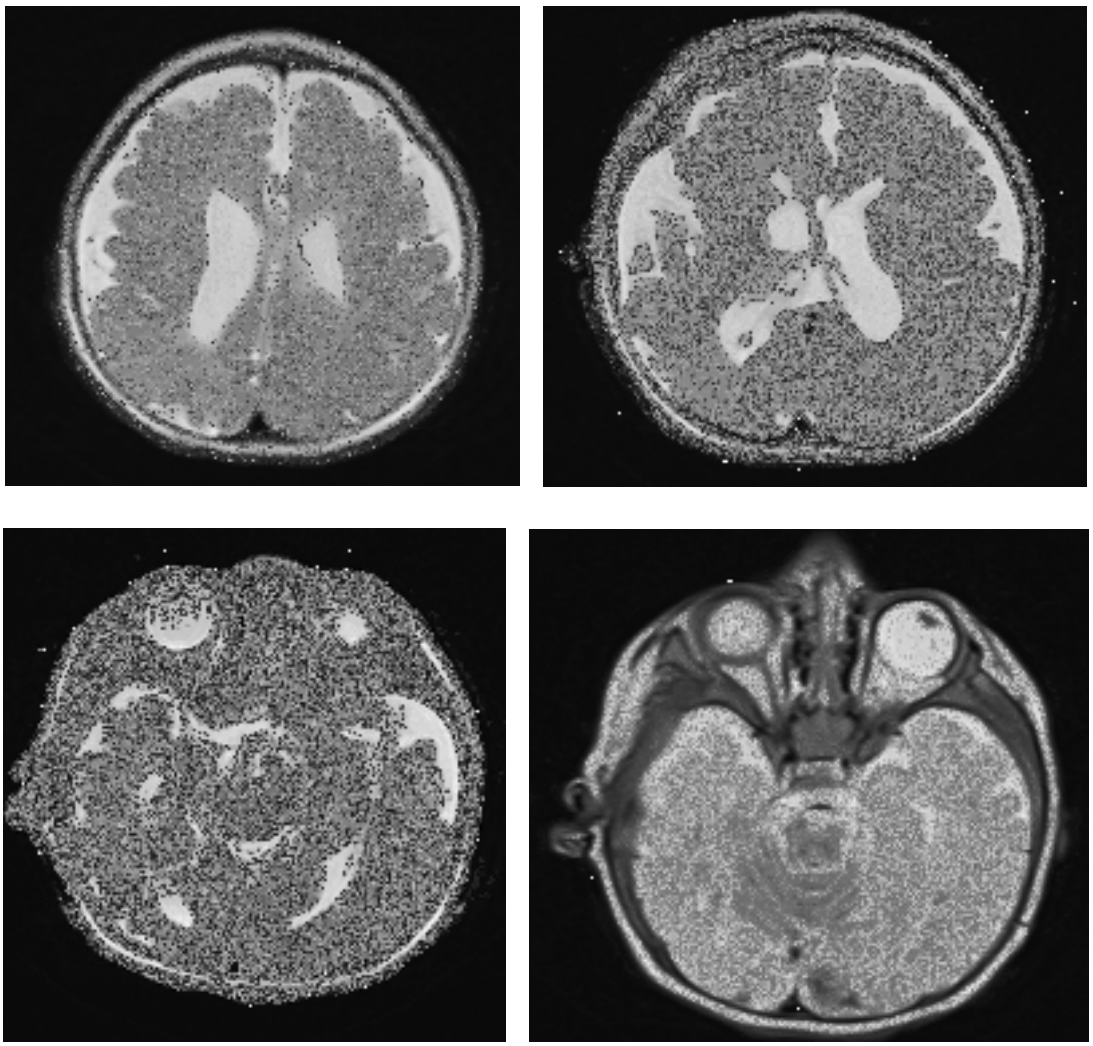


Figure 10.12, MPRAGE IMAGE

Case 11:

5month old male child presented with complaints of seizures since neonatal period , irritability and reduced vision. The child didn't cry immediately after birth. The child was 1st born out of non consanguineous marriage. There was complaints of developmental delay delay with no head holding, social smile, hand regard or recognition of mother. On examination, patient had alopecia, eczema, hyperpigmentation over ankles, post auricular rash and infantile spasm (15 clusters per day).The child was clinically diagnosed as biotinase deficiency \ holocarboxylase deficiency or mitochondrial disorder. MRI showed diffuse cerebral atrophy with corpus callosum dysgenesis and periventricular calcification .



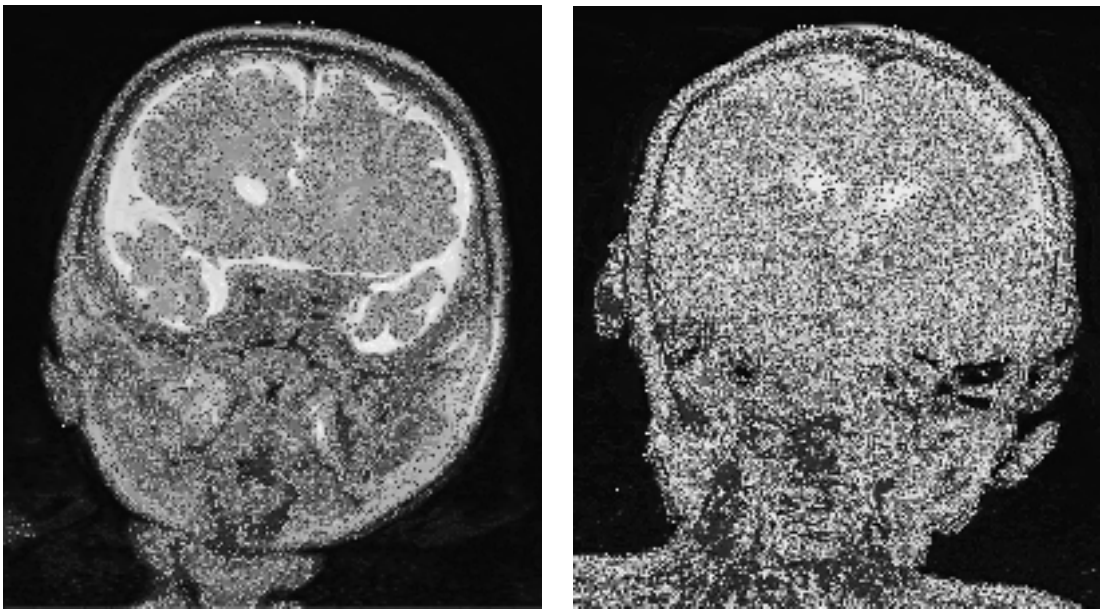


Figure 11.1, 11.2 , 11.3, 11.4 11.5 & 11.6 : T2 weighted images

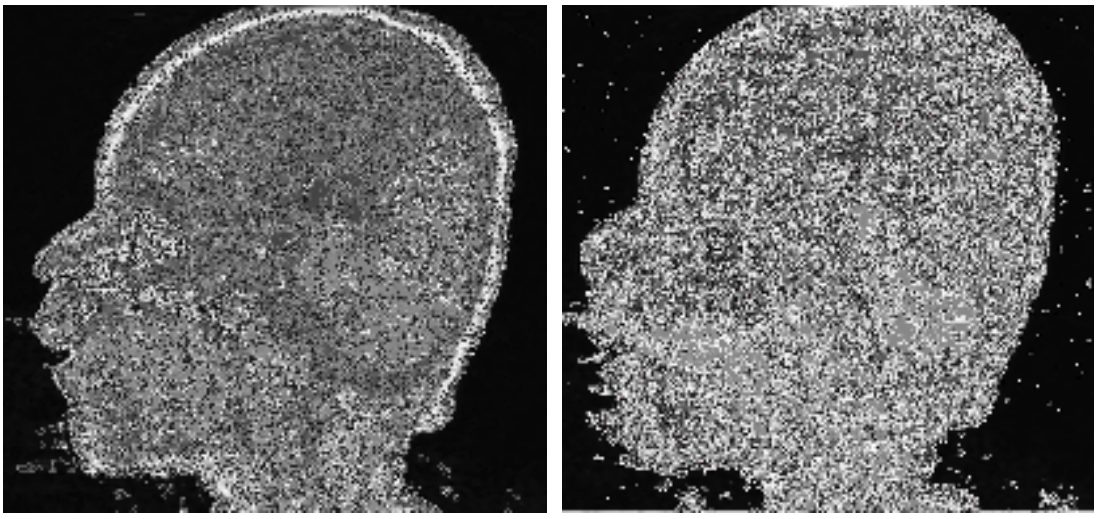


Figure 11.7 &11.8 : T1 sagittal images

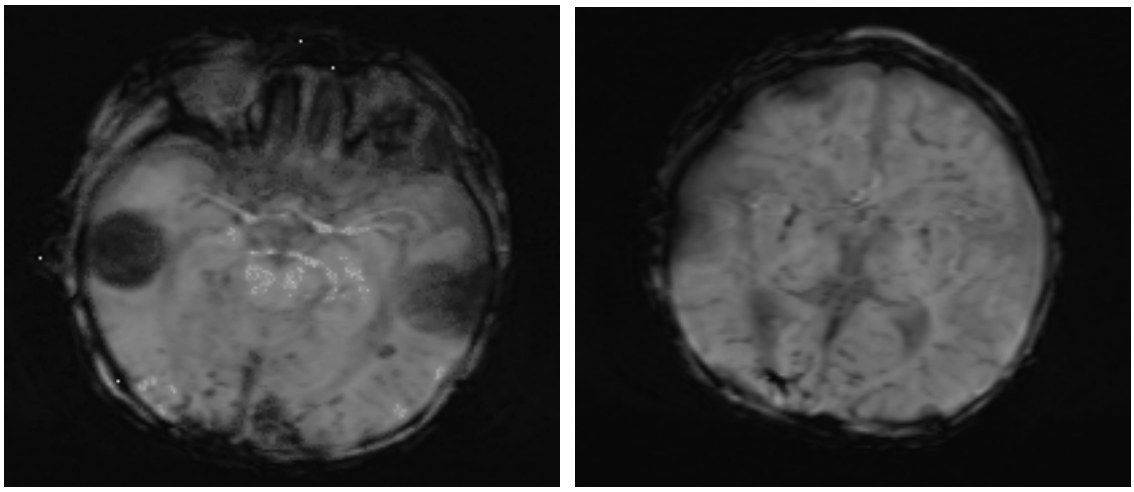


Figure 11.7 &11.8 :SWIl images

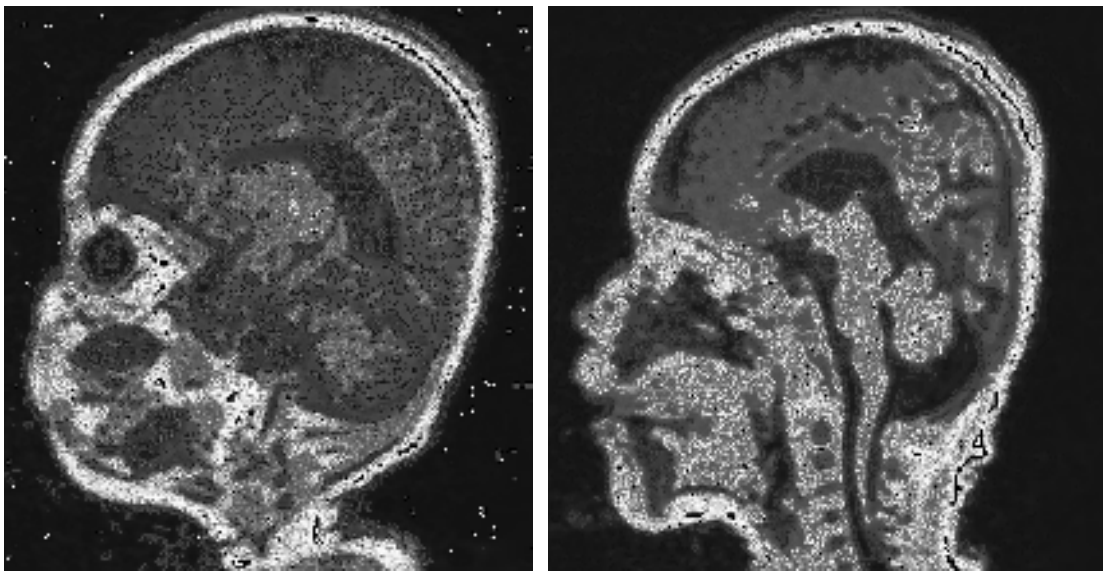


Figure 11.9 &11.10 : MPRAGE images

CASE 12 :

3year oldchild presented with episodes of hypoglycemia and developmental delay. On MRI there is hypoplasia of vermian with atrophy resulting in widening of folia.There is also associated atrophy of cerebellar lobes.There is increased FLAIR signals in cerebellar lobes.There is evidence of pontine atrophy. Radiologicalally and clinically the patient was diagnosed as congenital disorder of glycosylation.

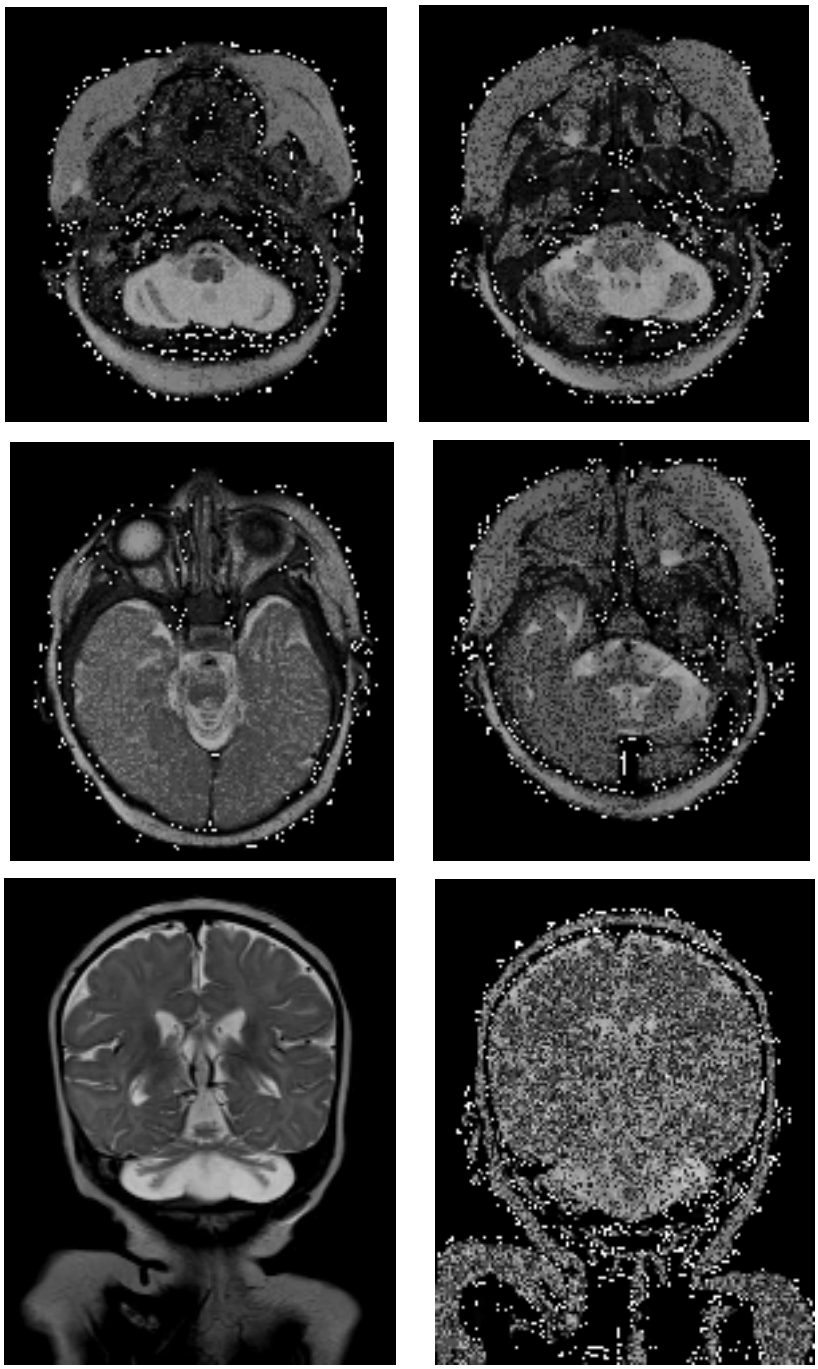


Figure 12.1 , 12.2 , 12.3 , 12.4 , 12.5 & 12.6 : Axial and coronal T2 weighted images

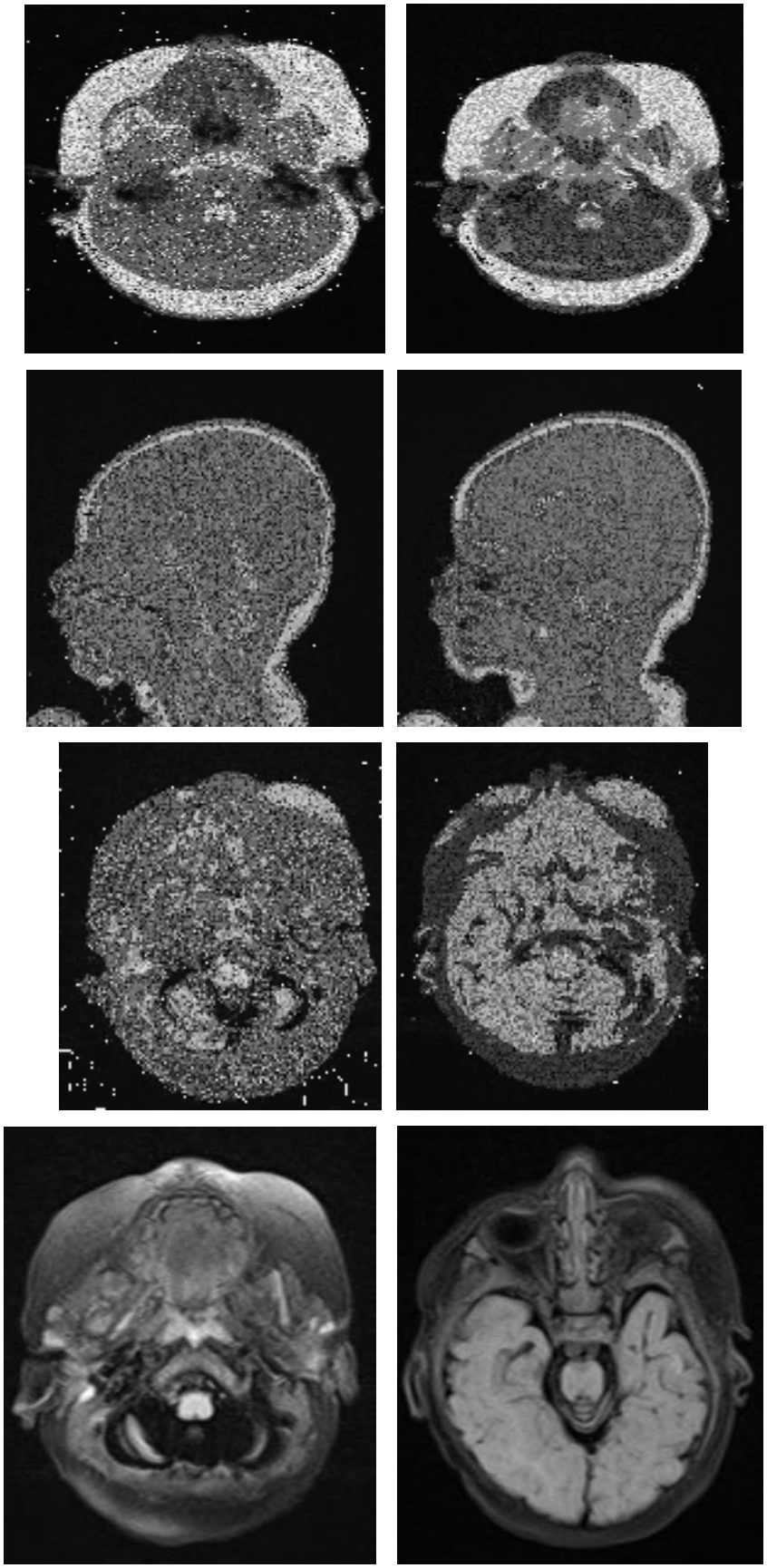


Figure 12.7 , 12.8 , 12.9 , 12.10 , 12.11 & 12.12: AXIAL T1 WI

ANNEXURE V - KEY TO MASTER CHART

1 : Yes/ Present

0 : No /Absent

M : Male

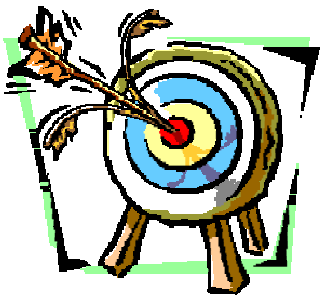
F : Female

ANNEXURE VI - MASTER CHART

Patient No	<1YEAR	1-3YEARS	3-5YEARS	>5YEARS	MALE/FEMALE	CEREBRAL PALSY	GDD/ID	AUTISM	OTHER	ONLYDEVELOPMENTAL DELAY	DEVELOPMENTAL DELAY +SEIZURES	DEVELOPMETAL DELAY +OTHER HISTORY	LSCS	LBW	PRETRM	NICU ADMISSION	CIAB	HYPOXIC INSULT	CONSANGIOUNOUS MARRIAGE	NORMAL HEAD SIZE	MACROCEPHALY	MICRCEPHALY	hypoxic ischemic insult	DEVELOPMENTAL ANAMALY	METABOLIC ANAMALY	POST INFECTION	NEOPLASTIC ETIOLOGY	NON SPECIFIC ETIOLOGY	NORMAL MRI	MAJOR ABNORMAL FINDINGS	MINOR ABNORMAL FINDINGS	COTICAL INVOLVEMNENT	WHITE MATTER INVOLVEMT	MEDIAL TEMPORAL LOBE INVOLVEMENT	VENTRICULAR INVOLVEMT	BASAL GANGLIA INVOLVEMENT	CORPUS CALLOSUM INVOVEMENT	BRAINSTEM	CEREBELLUM	DELAYED MYELINATION	MEGA CISTENA MAGNA	DILATED VR	CYSTS	cavum septum pellucidum/velum	ENLARGED SAS	PVL	SPECTROSCOPY
1	0	0	1	0	F	1	0	0	0	1	0	0	0	1	1	1	1	0	0	1	0	0	0	1	0	0	0	0	0	1	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0
2	0	1	0	0	M	1	0	0	0	0	0	1	0	0	0	1	0	1	0	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1
3	0	0	0	1	M	0	0	1	0	0	1	0	0	0	0	0	1	0	0	1	0	0	0	1	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0
4	0	1	0	0	M	1	0	0	0	1	1	0	0	0	0	1	1	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0
5	1	0	0	0	F	1	0	0	0	1	0	0	1	0	0	0	1	0	0	1	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
6	0	1	0	0	M	1	0	0	0	0	0	1	1	1	1	1	0	1	0	1	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	1	0	1	0	0	0	1	1	0	0	0
7	0	1	0	0	M	1	0	0	0	0	0	1	1	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	1	0	0	0
8	0	0	0	1	M	0	1	0	0	0	1	0	1	1	1	1	0	1	0	1	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0
9	0	1	0	0	F	1	0	0	0	1	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1	0	0
10	0	1	0	0	F	1	0	0	0	1	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11	0	0	0	1	F	1	0	0	0	0	1	0	0	0	0	0	1	0	0	1	0	0	0	1	0	0	0	0	0	0	1	0	1	1	1	0	0	0	0	0	0	0	1	0	0	0
12	0	0	1	0	M	1	0	0	0	1	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
13	1	0	0	0	M	1	0	0	0	0	1	0	0	0	0	0	1	0	1	1	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	1	0	0	0	1	0	0
14	0	0	0	1	M	0	1	0	0	1	0	0	0	0	0	0	1	0	1	1	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	1	0	1	0	0	0	0	1	0	0	0
15	0	1	0	0	M	1	0	0	0	0	0	1	0	1	1	1	0	0	0	1	0	0	0	1	0	0	0	0	0	0	1	1	1	1	1	0	1	0	0	0	1	0	0	0	1	1	0
16	0	0	1	0	M	1	0	0	0	0	1	0	0	0	0	0	1	0	0	1	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0
17	0	0	0	1	F	0	1	0	0	0	1	0	0	0	0	0	1	0	0	1	0	0	0	0	1	0	0	0	0	0	1	0	1	0	0	1	0	0	0	0	0	1	0	0	1	0	0
18	0	0	0	1	M	0	1	0	0	0	1	0	0	0	0	0	1	0	1	1	0	0	0	1	0	0	0	0	0	0	1	1	1	1	0	0	0	0	0	0	1	0	0	0	1	0	0
19	1	0	0	0	M	1	0	0	0	0	0	1	1	1	1	1	0	0	1	1	0	0	0	0	0	1	0	0	0	0	1	0	0	0	1	1	1	0	0	0	0	0	0	0	1	0	0
20	0	1	0	0	M	1	0	0	0	0	0	1	0	0	0	0	1	0	0	1	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0
21	0	1	0	0	F	1	0	0	0	0	0	1	0	0	1	0	1	0	0	1	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0
22	0	1	0	0	M	1	0	0	0	0	0	1	1	1	0	1	0	0	0	1	0	0	0	1	0	0	0	0	0	0	1	0	0	1	1	0	1	0	0	0	0	1	0	0	1	0	0
23	0	0	0	1	F	0	1	0	0	1	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	1	0	0	1	1	0	0	0	0	0
24	0	0	0	1	M	1	0	0	0	0	0	1	1	0	0	1	1	0	0	1	0	0	0	1	0	0	0	0	0	0	1	0	0	1	0	1	0	0	0	0	1	1	0	0	0	1	0
25	1	0	0	0	F	1	0	0	0	1	0	0	0	0	0	0	1	1	1	1	0	0	0	0	1	0	0	0	0	0	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0
26	1	0	0	0	M	1	0	0	0	1	0	0	1	1	1	1	1	1	1	0	1	0	0	0	0	1	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
27	0	0	0	1	F	0	1	0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	1	0	0	1	0	1	0	0	0	1	0	1	1	0	0	0	0
28	0	0	0	1	M	1	0	0	0	0	1	0	0	1	0	0	1	0	0	1	0	0	0	0	1	0	0	0	0	0	1	0	1	0	0	1	0	1	0	0	0	0	0	0	1	0	0
29	0	0	0	1	F	1	0	0	0	0	0	1	1	0	0	1	1	0	0	1	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
30	0	1	0	0	F	1	0	0	0	1	0	0	0	0	0	1	0	1	0	1	0	0	0	1	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
31	0	0	0	1	F	1	0	0	0	0	0	1	1	0	0	0	1	0	0	0	0	1	0	0	1	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0
32	0	0	1	0	M	0	0	0	1	1	0	1	1	1	0	1	1	0	1	0	0	1	0	0	0	0	0	1	0	1	1	0	0	0	1	0	0	0	0	1	0	0	0	1	0	0	0
33	0	0	0	1	M	1	0	0	0	1	0	0	0	0	0	0	1	1	0	1	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0
34	0	1	0	0	F	0	0	0	1	1	0	0	0	0	0	0	1	1	0	1	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
35	0	0	1	0	M	1	0	0	0	0	0	1	0	0	0	1	0	1	1	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
36	0	0	0	1	M	1	0	0	0	0	0	1	0	1	1	1	0	1	0	1	0	0	0	0	0	0	0	1	1	0	1	0	1	0	0	0	0	0	0	1	0	0	0	0	1	0	0
37	0	0	0	1	M	0	1	0	0	1	0	0	0	0	1	1	1	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

38	0	1	0	0	M	1	0	0	0	1	1	0	0	0	0	1	1	1	0	0	1	0	1	0	0	0	0	0	0	1	1	0	0	0	0	0	0	1	1	0	1	0	0	1	1	0	0
39	1	0	0	0	M	1	0	0	0	1	0	0	0	1	0	1	1	1	1	0	0	1	1	0	0	0	0	0	0	1	0	1	1	0	1	0	0	0	0	0	1	0	0	0	1	0	0
40	1	0	0	0	M	0	0	0	1	0	0	1	0	0	0	0	1	0	1	1	0	0	0	0	1	0	0	0	0	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
41	1	0	0	0	M	0	0	0	1	0	1	0	0	0	0	0	1	0	1	0	0	1	0	1	0	0	0	0	0	1	0	0	1	0	1	1	1	0	1	0	1	0	0	0	1	0	0
42	0	1	0	0	M	1	0	0	0	0	0	1	0	0	0	0	1	0	0	1	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
43	1	0	0	0	F	1	0	0	0	1	0	0	0	0	0	1	0	1	1	0	0	1	1	0	0	0	0	0	0	1	0	1	1	0	1	0	0	0	0	0	1	0	0	0	1	1	0
44	1	0	0	0	M	1	0	0	0	1	0	0	0	0	0	0	1	0	1	1	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0
45	0	1	0	0	F	1	0	0	0	1	0	0	1	1	1	1	0	0	0	1	0	0	0	0	0	0	0	1	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
46	0	0	0	1	M	1	0	0	0	0	0	1	0	1	0	1	0	1	0	1	0	0	0	1	0	0	0	0	0	1	0	0	1	0	1	0	1	0	0	0	0	0	0	0	0	0	0
47	0	1	0	0	F	0	0	0	1	1	0	0	0	0	0	0	1	0	0	1	0	0	0	0	1	0	0	0	0	1	1	0	0	0	0	0	0	0	1	0	1	0	0	1	0	0	0
48	0	0	0	1	M	1	0	0	0	0	0	1	0	0	0	1	0	0	0	1	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
49	1	0	0	0	M	1	0	0	0	0	1	0	0	0	0	1	0	1	1	1	0	0	1	0	0	0	0	0	0	1	0	1	1	1	1	1	1	0	0	0	0	0	0	0	1	1	0
50	0	1	0	0	M	0	0	0	1	0	0	1	1	1	0	1	0	0	1	1	0	0	0	1	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0
51	1	0	0	0	M	1	0	0	0	0	0	1	1	1	0	1	1	0	0	1	0	0	1	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	1	0
52	0	0	1	0	M	1	0	0	0	1	0	0	1	1	1	1	0	0	0	1	0	0	1	0	0	0	0	0	0	1	1	0	1	0	0	0	0	0	0	0	1	0	0	0	0	1	0
53	0	1	0	0	M	0	0	1	0	1	0	0	0	0	0	0	1	0	1	1	0	0	0	0	0	0	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
54	0	1	0	0	M	1	0	0	0	1	0	0	1	1	1	1	0	1	1	1	0	0	0	1	0	0	0	0	0	1	1	0	1	0	0	0	1	0	0	0	1	1	0	0	1	0	0
55	0	1	0	0	F	1	0	0	0	1	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
56	1	0	0	0	F	1	0	0	0	1	0	0	0	0	0	0	1	0	1	1	0	0	0	1	0	0	0	0	0	1	0	0	0	1	1	0	1	0	0	0	0	0	0	0	0	0	0
57	1	0	0	0	M	1	0	0	0	1	0	0	1	0	0	0	1	0	0	1	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	1	0	1	0	0	0	1	0	0
58	0	1	0	0	M	1	0	0	0	1	0	0	1	1	1	1	0	1	0	1	0	0	1	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	1	1	1	0
59	1	0	0	0	M	1	0	0	0	0	1	0	0	0	0	1	0	1	0	1	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
60	0	1	0	0	M	1	0	0	0	1	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
61	0	1	0	0	M	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
62	0	1	0	0	M	0	1	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
63	0	1	0	0	M	0	1	0	0	1	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
64	0	1	0	0	F	1	0	0	0	1	0	0	0	0	1	0	1	0	1	1	0	0	1	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	1	0	1	0	0	0	0	1	1
65	1	0	0	0	F	1	0	0	0	0	0	1	1	0	0	0	1	0	0	1	0	0	0	0	0	0	1	0	1	1	0	0	1	1	0	1	0	1	0	0	1	0	0	1	1	0	0
66	0	0	1	0	M	0	1	0	0	1	0	0	1	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1
67	0	0	0	1	M	0	0	0	1	0	1	0	0	0	1	1	0	0	1	1	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	1	0	0	1	0	0	0
68	1	0	0	0	F	1	0	0	0	1	0	0	0	0	0	1	1	1	1	1	0	0	1	0	0	0	0	0	0	1	0	1	1	1	1	0	1	0	0	0	1	0	0	1	1	1	0
69	0	1	0	0	M	1	0	0	0	0	1	0	0	0	0	1	1	0	0	1	0	0	0	1	0	0	0	0	0	1	0	1	1	0	1	0	1	0	0	0	0	0	0	1	1	1	0
70	0	1	0	0	M	0	0	0	1	1	0	0	0	0	0	0	1	0	0	1	0	0	1	0	0	0	0	1	0	1	0	0	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0
71	0	1	0	0	F	1	0	0	0	0	1	0	0	0	0	0	1	0	0	1	0	0	0	1	0	0	0	0	0	1	0	1	1	0	1	0	0	0	0	0	1	1	0	1	0	0	0
72	0	0	0	1	F	1	0	0	0	1	0	0	1	1	1	1	0	1	0	1	0	0	0	0	0	0	0	1	0	1	1	0	1	0	1	0	0	0	0	0	1	0	0	1	1	1	0
73	0	1	0	0	M	1	0	0	0	0	1	0	0	1	1	1	0	1	0	1	0	0	1	0	0	0	0	0	0	1	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	1	0
74	0	0	0	1	M	1	0	0	0	1	0	0	1	1	1	1	0	1	0	1	0	0	1	0	0	0	0	0	0	1	0	0	1	1	1	0	1	0	0	0	0	0	0	1	0	1	0
75	0	0	1	0	M	1	0	0	0	0	1	0	1	1	1	1	0	1	0	1	0	0	1	0	0	0	0	0	0	1	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	1	0
76	1	0	0	0	F	0	0	0	1	0	0	1	0	0	0	1	1	0	0	1	0	0	0	0	1	0	0	0	0	1	0	1	0	0	0	0	1	1	1	0	1	0	0	1	1	0	0
77	0	1	0	0	M	0	0	0	1	1	0	0	0	0	0	0	1	0	0	1	0	0	0	0	1	0	0	0	0	1	1	0	0	0	1	0	0	0	1	0	1	1	0	1	1	0	1
78	1	0	0	0	M	1	0	0	0	0	0	1	1	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0
79	0	1	0	0	M	0	0	1	0	0	1	0	0	0	0	0	1	0	0	0	0	1	0	0	1	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	1	1	0	0
80	0	1	0	0	M	1	0	0	0	1	0	0	1	1	1	1	1	1	0	1	0	0	0	0	1	0	0	0	0	1	0	1	1	0	1	0	0	0	1	0	0	0	0	1	1	0	0
81	0	0	0	1	M	1	0	0	0	1	0	0	0	0	0	0	1	0	1	1	0	0	0	1	0	0	0	0	0	1	1	0	0	0	0	0	0	1	0	0	1	0	0	0	1	0	0
82	1	0	0	0	M	1	0	0	0	0	0	1	0	1	0	1	1	0	0	1	0	0	1	0	0	0	0	0	0	1	0	0	1	0	1	0	0	0	0	0	1	1	0	0	0	1	0
83	1	0	0	0	M	1	0	0	0	0	0	1	0	1	0	0	1	0	0	0	1	0	0	0	1	0	0	0	0	1	1	1	1	0	1	0	0	0	0	0	1	0	0	1	1	0	0
84	0	1	0	0	M	1	0	0	0	1	0	0	1	1	0	0	1	0	0	1	0	0	0	1	0	0	0	0	0	1	1	0	0	0	1	0	1	0	0	0	0	0	0	1	0	0	0
85	0	0	0	1	F	1	1	0	0	0	0	1	0	0	0	1	0	0	1	0	0	1	0	1	0	0	0	0	1	0	0	1	1	0	1	0	1	0	1	0	0	0	1	0	0	0	0

Introduction



Objectives

Review of Literature

Methodology

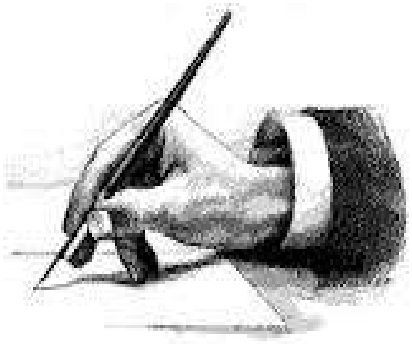
Results

Discussion

Conclusion

Summary

Bibliography



Annexure-I

Annexure-II

Annexure-III

Annexure-IV

Annexure-V

Annexure-VI