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The Value of Myelination Milestone on MRI in the Assessment of Developmental Delay in Pediatric Patients

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Abstract **Background**: Delay milestone is a common clinical problem in pediatrics, it present during infancy as developmental delay. Myelination is a dynamic procedure that starts with myelination of the most primary bits of the cerebrum. The study was performed in the MRI unit of AL-Emamain AL-Kadhimain medical city and, was conducted on 47 developmentally delayed children, 27 males and 20 females, who visited the pediatric outpatient unit in the period from October 2017 to June 2018, No etiological diagnosis could be made following clinical examination and primary investigations in all patients who enrolled in this study. **Objective**: To study MRI findings and myelination milestones in some children with delay development. **Results**: 21 patients had abnormal MR findings and 26 patients were with normal MRI examination where no abnormal findings could be noticed. According to MRI finding, we have been classified MR finding into various causes metabolic /degenerative 4.3 %, congenital and developmental 6.4 %, traumatic/neurovascular10.6%, non specific 23.4%, normal 59.6 %. **Conclusion**: MRI should be done to child with global developmental delay where no obvious etiology can be found after examination and proper investigations.

Keywords: *Myelination, MRI, developmental delay, pediatric*

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1. Introduction

1.1. Background

Development is a continuous procedure from conception till maturity, during this period many factors affect this procedure like environmental, nutritional and chronic disease, the assessment of child development is based on four aspects of gross motor, fine motor, social and language skills. Children who cannot achieve one or more of these developmental skills at the corresponding age but in a correct sequence compared with that of typically developing children, associated with sub average intellectual functioning (IQ < 75), have been diagnosed as developmental delay [1,2].

Developmental delay refers to a child when he/she does not achieve developmental milestone within the normal expected range of age [3].

Developmental delay does not suggest a particular organic diagnosis but rather a descriptive term used for children whose difficulties in developmental skills are obvious earlier in childhood, where a cause is not yet established [4]. Developmental delay is a common pediatric disorder with a prevalence of about 3-10% which interferes with physical activity in 16.7% of those affected [5]. The most common causes being: Metabolic, Genetic, Perinatal infections, Endocrine, and Toxins (Table 1) [6].

Initial recognition of such disorders is essential not only for diagnostic and prognostic purposes, but also for the initiation of possible early therapeutic interventions [7]. Diagnosis of developmental delay depends on history, physical examination, and assessing brain myelination [8].

1.2. Etiology of Developmental Delay

There are enumerable causes for the phenomena of developmental delay, these encompass traumatic, infectious, genetic, metabolic, vascular, malformation syndromes, endocrine, toxins and environmental among other causes, Table 1 lists the causes of developmental delay in detail [9].

Table 1. Etiology of Developmental Delay [19,20]

1- Neurulation (3 to 4 Weeks' Gestation)
• Anencephaly
• Encephalocele
• Myelomeningocele
• Chiari malformation
2- Prosencephalic Formation (2 to 3 Months' Gestation)
• Holoprosencephalics (Alobar, Semilobar, Lobar)
• Agenesis of corpus callosum
• Septooptic dysplasia
• Cerebellar hypoplasia /aplasia
• Dandy-Walker spectrum
• Craniosynostosis
3- Neuronal Proliferation (3 to 4 Months' Gestation)
• Microcephaly
• Macrocephaly (Soto syndrome)
• Neurocutaneous syndromes
• Vascular anomalies89o
• Arachnoid cyst
4- Neuronal Migration Disorders (4 to 5 Months' Gestation)
• Schizencephaly
○ Open cleft
○ Closed cleft
• Lissencephaly: pachygyria
• Heterotopias
5- Myelination Defects (5 Months' Gestation to 2 years)
• Hypomyelination
• Delayed myelination
• Dysmyelination
• Demyelination
• Cortical dysmaturity
6- Organizational Defects of the Central Nervous System (7 Months' Gestation to7 Years' Postnatal)
• Cortical dysgenesis
• Trisomy 21
• Fragile X
7- Idiopathic

1.3. Imaging in Developmental Delay

Proper approach and investigation can detect a definitive cause for developmental delay which can be identified in 40-85% cases with developmental delay [10,11].

Magnetic resonance imaging (MRI) is one of the important investigation tools of the children with delayed development [12].

Magnetic resonance imaging (MRI) is better than CT scan due to visualizing posterior fossa, lacking ionizing radiation, and improved contrast sensitivity permitting the assessment of central nervous system myelination. MRI is very sensitive to disease of the cerebral white matter [13]. MRI evaluate state of myelination both quantitatively and qualitatively [14,15]. MRI is the preferred method for approaching children with developmental delay [16].

Conventional MRI accurately characterizes brain organization and maturity, demonstrates malformations of the brain and spine, comprehensively assesses traumatic injury to the brain, and characterizes neoplastic, inflammatory, infectious, metabolic, and neurodegenerative disorders. Contrast enhanced MRI contributes additional information in the evaluation of vascular malformations, neoplasms, leukoencephalopathies, complications of meningoencephalitis, neuroendocrine disorders, and the characterization of CNS vascular morphology and patency [17,18].

1.4. Some Examples of MRI Characteristic Findings

Callosal agenesis: it accompanied with other congenital anomalies and may lead to seizures, moderate to severe mental retardation, hypothalamic disorders, impaired motor, bimanual or visual coordination and may be associated by midline craniofacial dysmorphy or macrocephaly [37]. (Figure 1)

Mucopolysaccharidoses: The mucopolysaccharidoses (MPS) is a group of heritable disorders caused by the lack of particular lysosomal enzymes engaged with the corruption and degradation of mucopolysaccharides, the mucopolysaccharidoses are ordered into six groups, which are additionally subdivided based on hereditary, biochemical, and clinical findings [38].

The MRI abnormalities consist of multiple small spot like lesions scattered in the white matter, with a predilection for the parietal and occipital white matter. The signal intensity follows the signal intensity of CSF; demonstrate the cystic nature of the lesions [38].

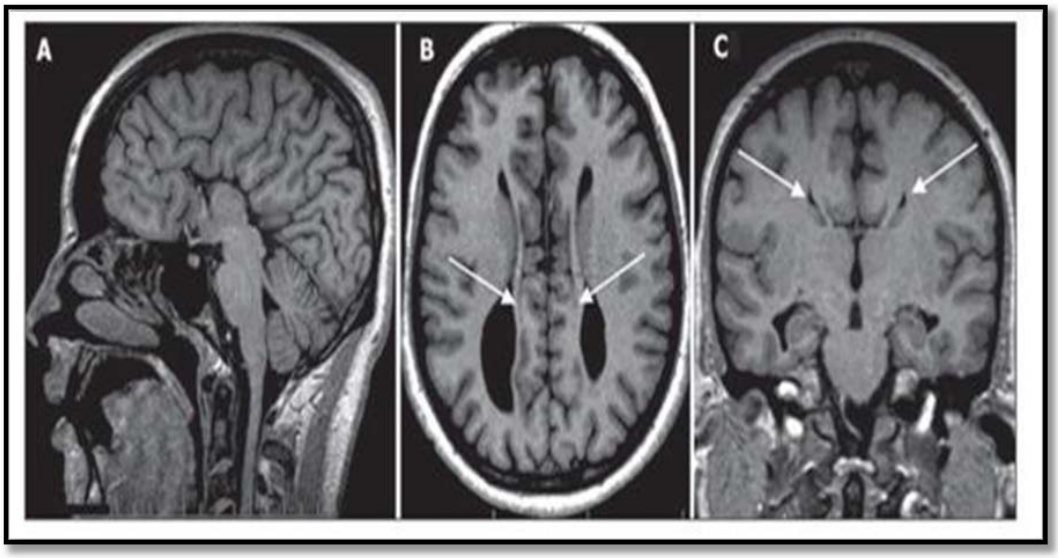

Figure 1. Callosal agenesis, (A) Mid sagittal view shows complete callosal agenesis;(B)Axial view shows the non-decussating fibers bundles of Probst (medial to the bodies of the 3rd ventricle-white arrow(C) coronal view show the classic "bat wing "appearance of the lateral ventricles-white arrows [41]

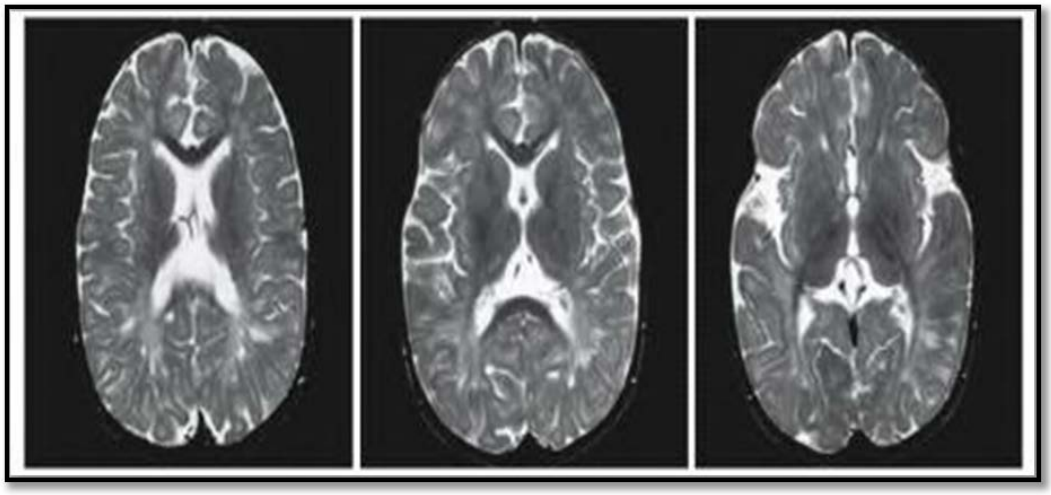

Figure 2. Mucopolysaccharides a 3 years old male with HURLER syndrome (MPS I). T2 weighted images confirm the enlarged periventricular spaces and show areas of high signal intensity. Courtesy of Dr. S. Blaser, Department of Diagnostic Imaging Hospital for Sick Children, Toronto [38]

Likewise, T2-weighted and FLAIR pictures may demonstrate multifocal smaller and bigger hyperintense regions, the signal intensity of which does not follow that of CSF. MRI may demonstrate a delay in myelination in young kids. Another common observation is ventricular enlargement, with or without associated subarachnoid spaces enlargement. Some patients seen to have extended CSF spaces based on diffuse atrophy of the brain parenchyma Figure 2 [38].

Neuronal heterotopias: MR is the investigation of choice to describe the ectopic clusters of neurons. Represented by seizures and different stages of developmental and neuropsychological status from normal to mild or severe delay. Heterotopic gray matter does not enhance after contrast infusion Figure 3 [37].

Phenylketonuria: Is an autosomal recessive disorders. Infants are normal at birth. Throughout the first year of life psychomotor retardation becomes obvious. Seizures may happen. The kids are little and frequently microcephalic. With Magnatic Resonance Imaging the earliest and commonest abnormalities comprise of high-signal intensity on T2-weighted images in the parieto-occipitalperiventricular white matter [39].

In more serious cases, the frontal periventricular white matter is also included and the white matter anomalies may stretch out into the subcortical area, specifically in the posterior area. The corpus callosum is almost, however not in every case totally spared Figure 4 [39].

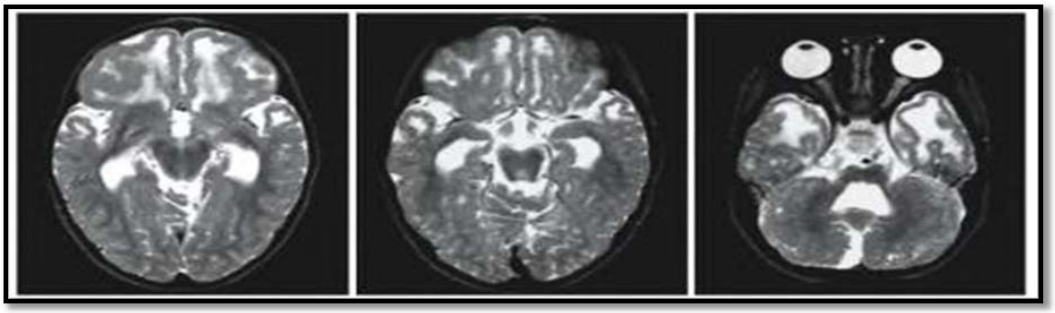

Figure 3. Neuronal heterotopias. 2.5 years old female, shows the irregular, thick frontal and temporal abnormal cortex, pachygyria polymicrogyria. Neuronal heterotopias are seen in the white matter along the lateral ventricles [42]

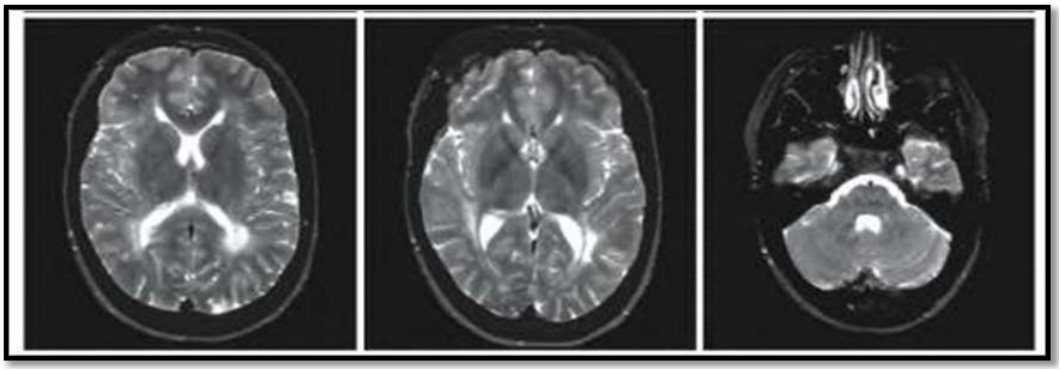

Figure 4. phenylketonurea patient presented with classical PUK there is a more prominently abnormal signal in the white matter bordering he frontal and especially, the posterior horn of the lateral ventricles [39]

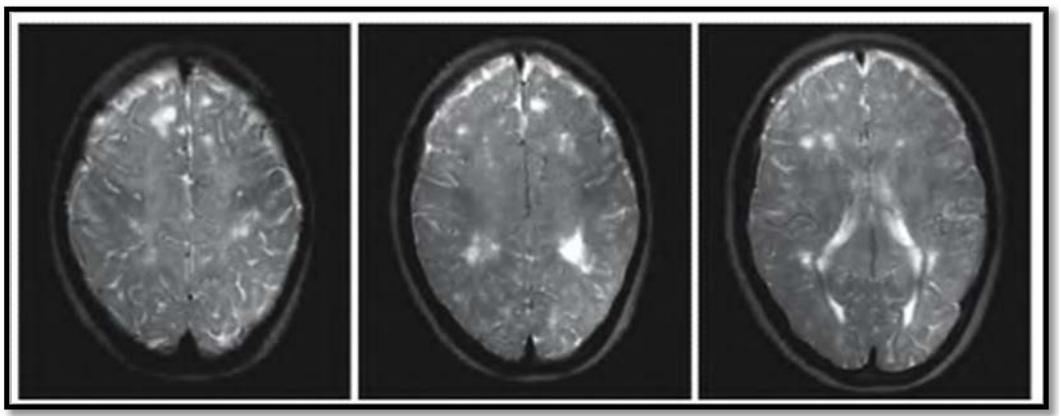

Figure 5. Galactosemia girl of 14 years old with galactosemia type 1. The T2 –weighted images show a combination of hypomyelination and patchy high signal intensity white matter abnormalities consistent with gliosis [40]

Galactosemia: All three kinds have an autosomal recessive mode of inheritance. A few patients are seen later in the first year of life because of retarded psychomotor development, cataracts, and hepatomegaly. Throughout the years, verbal and performance IQ gradually decrease, and a generous number of patients have lower than normal intelligence. with Magnetic Resonance Imaging: The primary abnormality observed by MRI is that after normal basic myelination the direct subcortical white matter does not move toward becoming hypointense on T2-weighted images as in normal kids older than 1 year, showing hypomyelination Figure 5 [40].

1.5. Myelination

The oligodendroglia cells of the focal sensory system supply the myelin. Giving both basic help and sustenance, the myelin additionally has a critical insulative property that enables electrical motivations to be directed with the physiologic speed important to advance neurologic capacity. [27]

Myelination is a dynamic procedure that starts with myelination of the most primary bits of the cerebrum. The phylogenetically most old parts, for example, the brain stem are normally completely myelinated at the time of birth.The main myelination is viewed as ahead of schedule as the sixteenth week of pregnancy, in the column of Burdach, however just truly set out at the 24th week [28].

Myelination relates nearly to developmental milestones [29]. The advancement of myelination is committed and complied with a simple generalized principles; myelination advances from: [30]

1. central to peripheral
2. caudal to cranial
3. dorsal to ventral
4. Sensory then motor

1.6. Phases of Normal Cerebral Myelination

Dietrich portrayed a three-grade myelination procedure:

The first grade, the infantile stage, from delivery to 8 months of age, is observable for the signal of the white matter, which is of higher intensity in comparison with the grey matter of cortex. This relation will be inverted by the adult stage. The tracts that are handling the more essential sensory input are the first to myelinate [27].

During childbirth, the medulla, dorsal midbrain, and cerebellar peduncles appear in any event some proof of myelination [27].

By 3 months of age, the cerebellum is totally grown-up like in appearance, even of the still developing cerebrum. The back part of the internal capsule displays myelination and a diminishing signal intensity upon the thicker part as the myelination procedure finishes. This is followed by the occurrence of myelination in the anterior internal capsule in about 2 to 3 months. The majority of the clarified changes happen while reviewing the TI-weighted images [27].

The corpus callosum, the biggest of the commissural fibers likewise develops in a posterior to anterior form. The evidence of myelination is found in the splenium by six months and in the genu by eight months [27].

The second grade, from 8 months to one year of age, is a transient period of isointensity where the grey and white matter are almost comparative in the signal intensities. While examining the T2-weighted images, the greater part of the profound white matter tracts have diminished in signal or be the opposite of the infantile pattern at 8 to 12 months. Once more, myelination is noted to continue in the posterior to anterior pattern. Utilizing a structure, for example, an internal capsule as a reference, the posterior limb thickens to about its most extreme measurment by 10 months. The anterior limb is on ways into its entire myelination process by II months [27].

The third, grown-up or adult, stage has been subdivided into an early adult grade, which stretches out from 12 to 31 months of age, and at that time the myelination mostly has already being finished, with the exception of the association zone of the centrum semiovale. The myelination follows a certain way. It advances from the caudal to the cephalad and from the dorsal to the ventral, implying that the occipital region myelinates before the frontal and that the brain stem myelinates before the hemispheres [27].

The region of the white matter in the centrum semiovale, near the ventricular trigone, shows the most postponed changes and uncrossed signal intensity can be noted into the first and second decades of life. This is a region of a large number of neurons involved in association tracts and referred as the terminal zone

territory with countless required with affiliation tracts and is additionally alluded to as the terminal zone. This zone can keep up with increase signal in an ordinary circumstance well into the 20s and this is considered as a normal finding rather than a demyelination. In the assessment of white matter development, the first 2 years of life are seem to be the most critical and important, with just unpretentious development changes seen from the third year into the second decade [27].

1.7. Assessment of Myelination

There are two methods to assess brain myelination: invasive -brain biopsy histology, or noninvasive – neuroimaging [27].

MRI in normal myelination

Utilizing magnetic resonance imaging (MRI) assessment of the white matter tract development need comprehending that the Tl-and T2-weighted imaging, which shows relaxation values, is straightforwardly identified with the measure of water content inside the cerebrum. In the immature brain, the free water content is increased [27].

During the procedure of myelination, the water will attach and the water- to-macromolecule proportion changes, which diminishes the relaxation values and make the maturing form and the adult form seen in typically normal development [27].

Myelination of the cerebrum through development advances in a precise and unsurprising style which can be evaluated with MRI. (Table 2).

Table 2. Normal MRI myelination progression

Region	T1	T2
Internal capsule Posterior limb	36 wk gestation	40 wk gestation
Posterior portion Posterior limb	First month	4-7 mo
Anterior portion Anterior limb	2-3 mo	7-11 mo
Corpus callosum Splenium	3-4 mo	4-6 mo
Corpus callosum Genu	4-6 mo	5-8 mo
White matter occipital	3-5mo (4-7mo subcortical)	9-14mo (11-15mo subcortical)
white matter Frontal	3-6mo (7-18mo subcortical)	11-18mo (14-30mo subcortical)
Centrum semiovale	2-4 mo	7-11 mo

1.8. Myelin Disorders: Definitions

'Demyelination' implies: loss of myelin and the exacting understanding of 'demyelinating disorders' is: disorders distinguished by myelin loss. The term demyelination is generally used to demonstrate the way toward losing myelin, which is caused by primary involvement of oligodendroglia or myelin membrane. Myelin loss that is secondary to axonal loss and synchronous loss of axons and myelin sheaths is not usually included under the heading of demyelination. Examples: metachromatic leukodystrophy, multiple sclerosis [36].

It has been confirm in a group of kids with hydrocephalus, in whom MRI and neuropsychological information were acquired previously and twice after shunting. There was a solid relationship between (a) the advancement of myelination in comparison with the normal myelination standard and (b) the progression of mental development in comparison with the normal developmental standard. It is necessary to follow up the advancement of myelination in any child in whom a delay is suspected, to see when, the kid makes up for normal myelination. It may be expected that a longer delay in the rebuilding of the typical form of myelination would correspond with a poorer prognosis [36].

There are numerous conceivable reasons for a demyelination: hypoxia– ischemia, congenital infections, congenital malformations, chromosomal abnormalities, congenital heart failure, postnatal infections, hydrocephalus, hypothyroidism, hypercortisolism, hypocortisolism, fetal intoxication, malnutrition and inborn error of metabolism. The delay is usually bilateral and symmetrical, however unilateral delay is found in cases with hemimegalencephaly, unilateral porencephalic cysts, cerebral hemiatrophy, or unilateral periventricular leukomalacia [36].

The important time in myelination development was at first believed to be simultaneous with the proliferation of myelin-forming cells, rather than with the time of membrane accumulation [36].

'Hypomyelination' is termed for conditions with a critical permanent deficiency in myelin deposit. The most extreme variant of hypomyelination is amyelination. Like in Pelizaeus-Merzbacher disease [36].

'Dysmyelination', as the exacting interpretation of the name infers, is named for conditions in which the procedure of myelination is impede or delayed, leading to abnormal patchy, irregular myelination, but not necessary accompanied by myelin loss. For example: some amino acidopathies, harmed structure of unmyelinated white matter after perinatal hypoxia or encephalitis [36].

'Retarded myelination' is used for disorders in which the deposit of myelin is delayed, but advancing, Examples: inborn errors of metabolism with early beginning, malnutrition, hydrocephalus [36].

'Myelin abnormalities' involve all the previously mentioned conditions.

'White matter disorders' and 'leukoencephalopathies' can be characterized as all the conditions in which dominantly and exactly affect the white matter. Either myelin or a blend of myelin and other white matter ingredients is included. Thus, white matter disorders are comprising all myelin disorders, but in addition, for example, white matter infections and infarctions, which may influence different white matter segments nonspecifically [36].

'grey matter disorders' contain all disorders in which neurons and axons are mainly or solely influenced [36].

Irregular myelination with local or generalized hypermyelination, or myelination that not following the ordinary courses of advancement, is uncommon, however is seen periodically. Hypermyelination, or advanced myelination has been seen in patients with Sturge-Weber syndrome. It has been thought that epileptic seizures may stimulate myelination. Anyway advanced myelination or hypermyelination isn't seen in many patients with infantile types of epilepsy [36].

1.9. Aim of the Study

The purpose of this study is to study and classify brain MRI findings by trying to establish a specific diagnosis when possible with the aid of myelination milestone.

2. Patients and Methods

2.1. Study Design

A cross-sectional study was performed in the MRI unit of AL-Emamain AL-Kadhimain medical city and, was conducted on 47 developmentally delayed children, 27 males and 20 females, their ages range from 1 month to 14 years. The study has been approved by the Ethical Committee of Institutional Review Board for Medical Research.

2.2. Inclusion Criteria

Every child complaining from delayed milestones of development and/or poor school performance who visited the pediatric outpatient unit in the period from October 2017 to June 2018 was eligible for enrollment in this study.

2.3. Exclusion Criteria

i. Any patient with previous history of CNS infections likemeningitis.
ii. Any patient with the following contraindications is excluded fromthis study:
   - Contraindications to MRI, including: metallic foreign body, implanted hearing aids.
   - Contraindications to sedation exist and include:
   - Airway obstruction
   - Respiratory centre lesions— for example, brain stem tumors
   - Renal or hepatic dysfunction leading to altered drug kinetics

2.4. Clinical Data

Every patient was assessed and examined clinically by pediatrician and printed data sheet on clinical aspects was filled. These clinical data include age, gender, age at diagnosis, known disease, past medical history, abnormal faces, and nature of developmental delay (motor, language, school difficulty).

Clinical presentation was classified into many categories including:

Developmental delay, developmental delay plus seizure, developmental delay plus autism, and developmental delay plus abnormalfacial or skeletal features.

2.5. MRI Technique

Brain MRI scans were performed using conventional 1.5-Tesla unit MAGNATOM avanto (Siemens medical system, Germany). All scans were taken in supine position using head coils.

Sedation with oral chloral hydrate, or IV Ketamine (50 mg /ml in a dose of 1-2 mg/kg over 1 minute, was used for the majority of patients (38 patients-young or claustrophobic were given swedation, 14 of them took IV Ketamine and the other 24 had oral chloral hydrate). No Gadolinium based contrast was needed.

Image protocol:

1. Axial T2 weighted (25 slices)with TR 5730 ms, TE 115 ms, FOV 200 mm, and Slice thickness 5 mm.
2. Sagittal T1 weighted (23 slices)with TR 232 ms, TE 4.76 ms, FOV 214mm, and Slice thickness 4 mm.
3. Coronal fluid attenuated inversion recovery (FLAIR) (25 slices) with TR 8100 ms, TE 102 ms, FOV 200 mm, and Slice thickness5 mm.
4. Axial Diffusion Weighted Image (DWI) (19 slices) with TR 3700ms, TE 114 ms, FOV 230 mm, and slice thickness 5 mm.
5. T1 weighted axial spin echo (27 slices) with TR 509 ms, TE 9.7 ms, FOV 200 mm, and slice thickness 4 mm.
6. T2 STIR axial (30 slices) with TR 489 ms, TE 18 ms, FOV 180mm, and slice thickness 4mm.

Imaging findings were categorized into:

1. Normal
2. Traumatic/neurovascular
3. Congenital/developmental
4. Non specific

Myelination milestones were categorized into

1- Normal
2- Delayed

2.6. Statistical Methods

The data was analysed y using PC software of the Statistical Package for the Social Science (SPSS) version 20.0. Cross-tabulation analysis used to test the significant association between categorical variables. A P- value of < 0.05 was been considered to indicate the level of significance throughout the study.

3. Results

Brain MRI was performed on 47 developmentally delayed children. They were 27 males and 20 females with male: female ratio of 1.3: 1 Mean ± SD = 3.7 ± 3.3 Y.

Patients were categorized into four age groups: <1 year, 1 to 3 years, 3 to 6 years, and 6 to 14 years. Most of cases were infants (29.8%) as shown in Table 3. There was no significant association between age category and gender of patients ($P > 0.05$).

Regarding clinical presentation of patients, 63.8% presented with only developmental delay (DD), 17% presented with DD plus seizure, 10.6% presented with DD plus autism, and 8.5% presented DD with plus abnormal looking.

Results of MRI study were normal in 55.3% of cases. There is significant association between MRI category and clinical presentation as shown in Table 4 (P = .01).

Table 3. age and sex distribution of patients*

			Age				Total
			less than 1 year	1-3 y	3-6 y	6-14	
Sex	male	Count	9	6	8	4	27
		% of Total	(19.1%)	(12.8%)	(17.1%)	(8.5%)	(57.4%)
	fema le	Count	5	6	5	4	20
		% of Total	(10.6%)	(12.8%)	(10.6%)	(8.5%)	(42.6)
		Count	14	12	13	8	47
Total		% of Total	(29.7%)	(25.6%)	(27.7%)	(17.0%)	(100.0%)

**P = .847,* Age range = 1 M -14 Y, Mean ± SD = *3.7 ± 3.3 Y.*

Table 4. MRI categories according to clinical presentation

			MRI_categories		Total
			norm al	abnorma l	
Clinical presentation	developmental delay	Count	17	13	30
		% of Total	36.2%	27.7%	63.9%
	developmental delay plus seizure	Count	1	7	8
		% of Total	2.1%	14.9%	17.0%
	developmental delay plus autism	Count	5	0	5
		% of Total	10.6%	0.0%	10.6%
	developmental delay plus abnormal facial or skeletal features	Count	3	1	4
		% of Total	6.4%	2.1%	8.5%
Total		Count	26	21	47
		% of Total	55.3%	44.7%	100.0%

*P=.01.

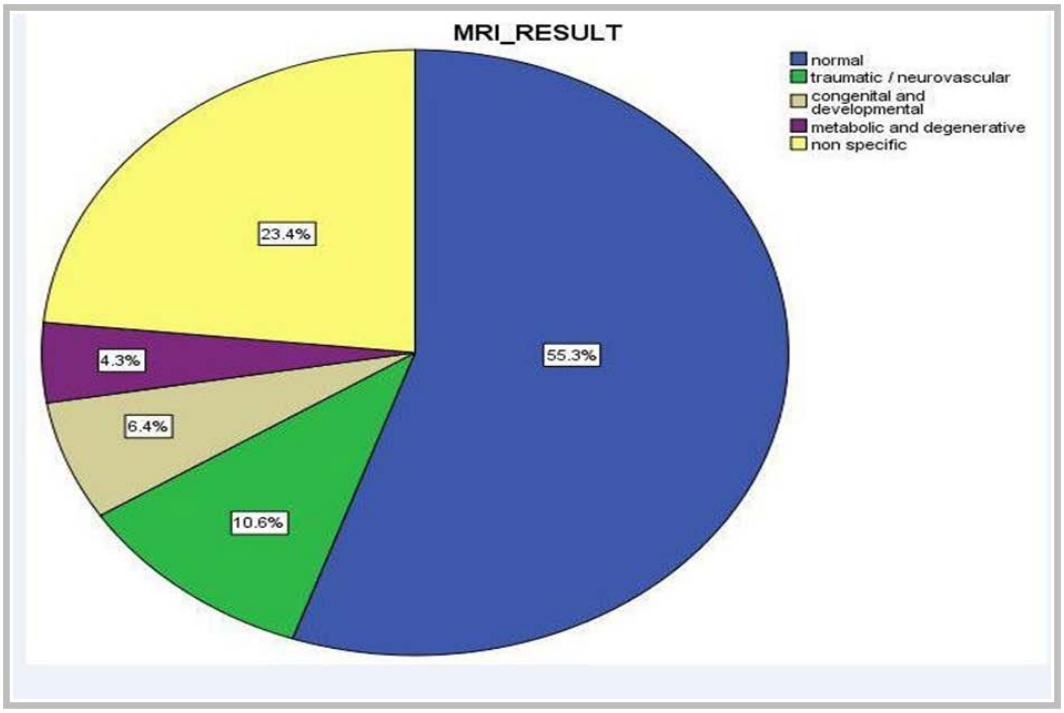

Figure 6. Categories of MRI results

The most common abnormal MRI finding was non-specific (23.4%), then the traumatic/ neurovascular (10.6%), congenital and developmental was (6.4%), and the least one was the metabolic and degenerative which was (4.3%), as shown in Pie chart in Figure 6.

Anatomy of involved structures in patients with abnormal MRI is shown in Table 5, and indicated that corpus callosum is the most common site (31.9%) which was mainly corpus callosum diffuse thinning, the second most common site was ventricular abnormalities either in morphology, size or both of them, it was about (21.3%).

Table 5. MRI findings in relation to anatomical structures

Anatomical structure	NO.	%
Ventricles	10	21.3
White matter	7	14.9
Gray matter	2	4.2
Corpus callosum	15	31.9
Brain stem	1	2.1
Cerebellum	1	2.1
Normal	28	55.3

Delayed myelination milestones occur in 12.8 % of patients, and 66.7% of them were infants and females (Table 6, Table 7), But there is no significant association between age and gender with myelination milestones (P = .15 and P = .20, respectively).

Table 6. distribution of myelination milestones according to gender

			sex		Total
			male	female	
Myelination milestones	normal	Count	25	16	41
		% of Total	53.2%	34.0%	87.2%
	delayed	Count	2	4	6
		% of Total	4.3%	8.5%	12.8%
Total		Count	27	20	47
		% of Total	57.4%	42.6%	100.0%

P=.15.

Table 7. distribution of myelination milestones according to age

			Age				Total
			less than 1 year	1-3 y	3-6 y	6-14	
Myelination Milestones	normal	Count	10	11	13	7	41
		% of Total	21.3%	23.4%	27.7%	14.9%	87.2%
	delayed	Count	4	1	0	1	6
		% of Total	8.5%	2.1%	0.0%	2.1%	12.8%
Total		Count	14	12	13	8	47
		% of Total	29.8%	25.5%	27.7%	17.0%	100.0%

P=.20.

There is significant association between clinical presentation and delayed myelination milestones *(P =.003)*. There is significant association between clinical presentation and delayed myelination milestones *(P =.003)* whereas 66% of delayed myelination milestones was from group of patient that presented with associated seizures and 0% was from group of patients that presented with autism.

Table 8. association between myelination milestones and clinical presentation*

			Clinical presentation				Total
			developmental delay	developmental delay plus seizure	developmental delay plus autism	developmental delay plus abnormal facial or skeletal features	
Myelination	Normal	Count	29	4	5	3	41
		% of Total	61.7%	8.5%	10.6%	6.4%	87.2%
milestone	Delayed	Count	1	4	0	1	6
		% of Total	2.1%	8.5%	0.0%	2.1%	12.8%
Total		Count	30	8	5	4	47
		% of Total	63.8%	17.0%	10.6%	8.5%	100.0%

*P = .003.

Myelination milestones is significantly associated with MRI results *(P = .004)*, Table 9 showed the association between MRI results and myelination milestones, which shows that (4.3%) of congenital/developmental as well as traumatic /neurovascular and non specific, have delayed myelination milestones, and 0% of patient with metabolic/degenerative abnormality have delayed myelination milestones, also 0% of patient with normal MRI results have delayed myelination milestones.

Table 9. myelination milestones in relation to MRI results

Myelination mile stone	MRI Results (% of total)					Total
	Normal	Traumatic/neurovascular	Congenital/developmental	Metabolic/degenerative	Non specific	
Normal	55.3%	6.4%	2.1%	4.3%	19.1%	87.2%
Delayed	0	4.3%	4.3%	0%	4.3%	12.8%
Total	55.3%	10.7%	6.4%	4.3%	23.4%	100%

*P=.004.

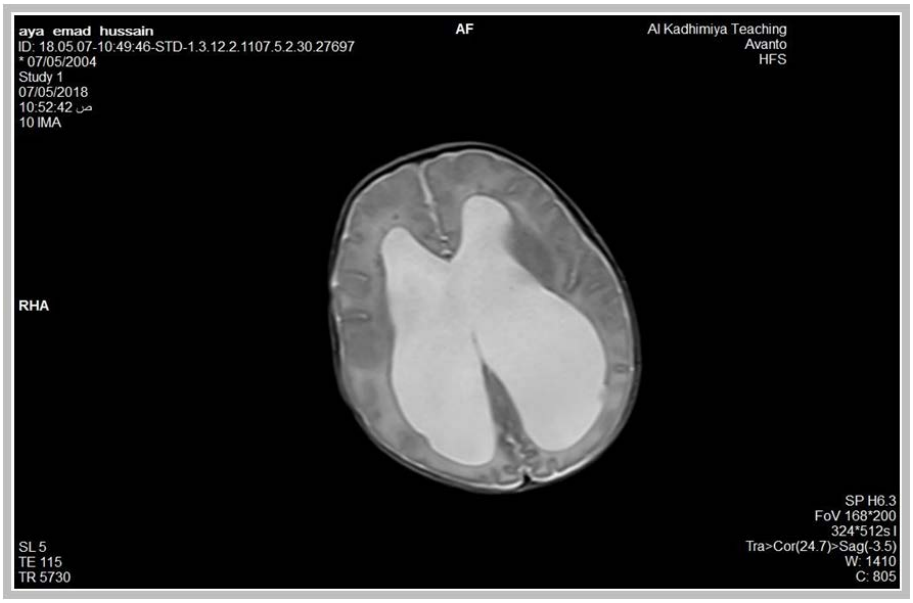

Figure 7. A 14 years old female patient, axial T2 WI shows colpocephaly

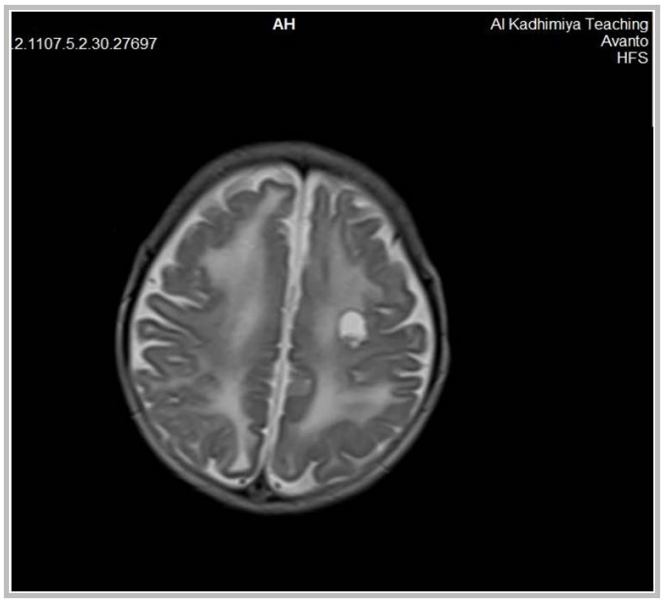

Figure 8. A 3 months old male patient, T2 weighted axial section shows bilateral encephalomalacia and hemorrhagic cystic lesion at the left parietal white matter

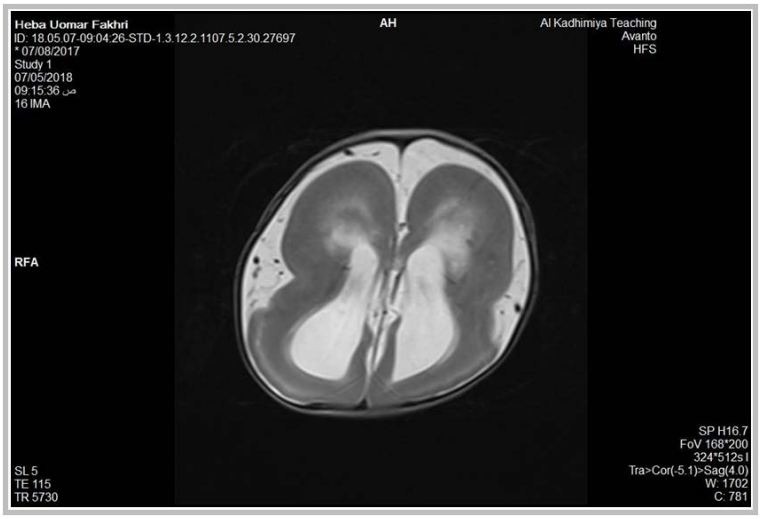

Figure 9. 9 months old female, T2 weighted axial section shows lissencephaly

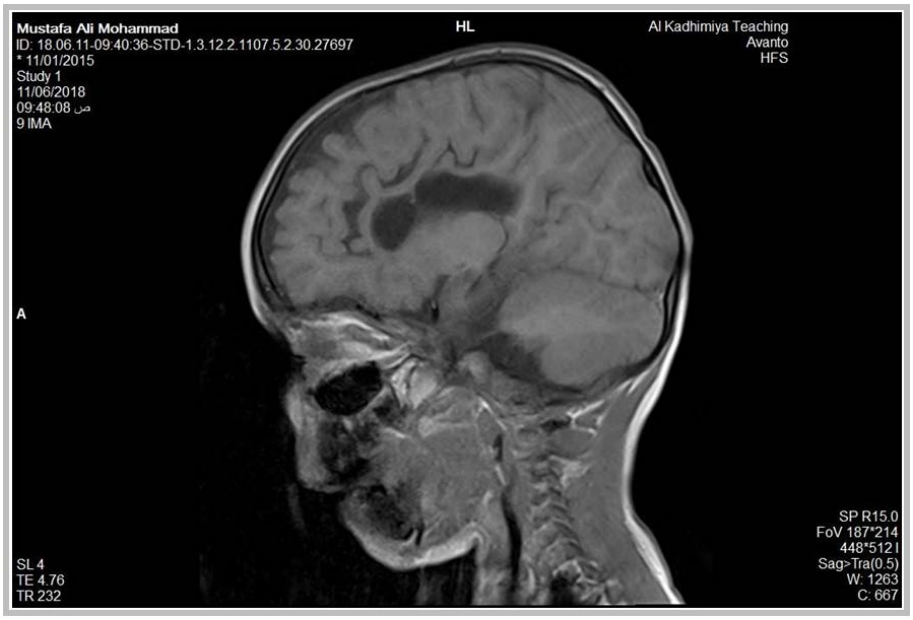

Figure 10. 3.5 years old male patient, T1 weighted para-sagittal section shows loss of white matter and atrophic gyri.

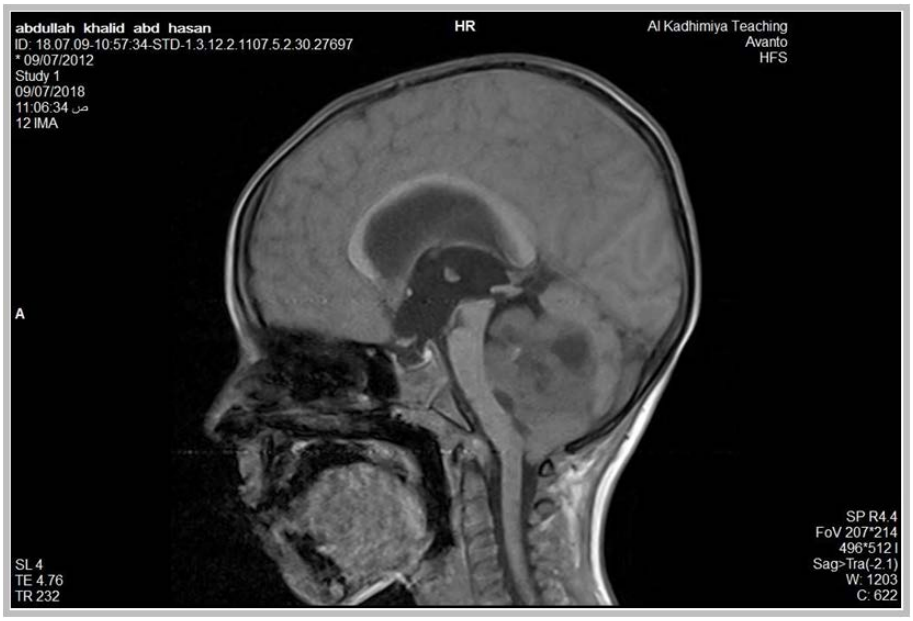

Figure 11. A 6 years old male patient, T1 WI sagittal section of brain MRI shows large 4th ventricular mass lesion filling the fourth ventricle cavity and effacing the brainstem with anterior compression, evidence of obstructive hydrocephalus with dilatation of the third and lateral ventricles

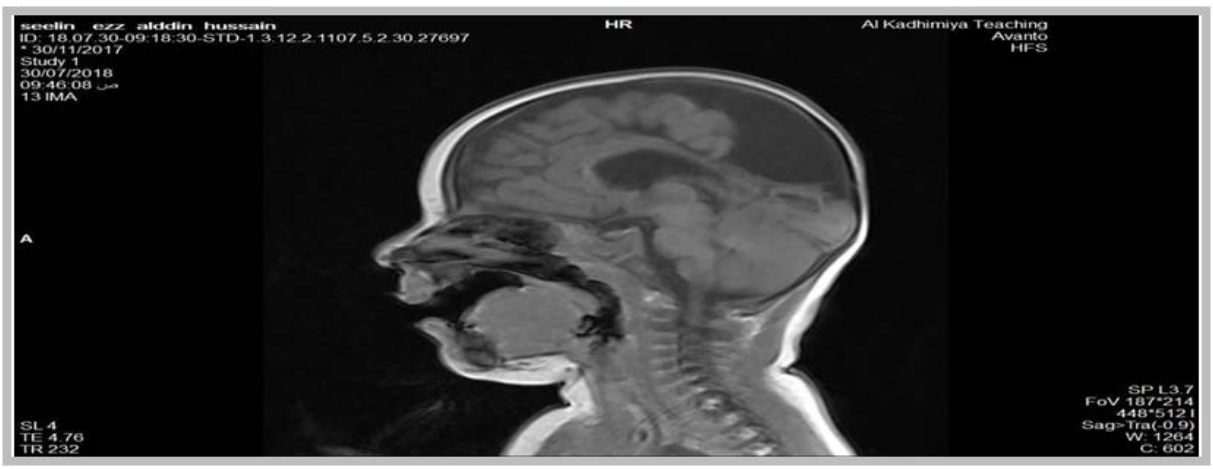

Figure 12. An 8 months old female patient, a midline sagittal image of T1 MRI shows marked loss of the parieto-occipital lobes with atrophy, and expansion of CSF spaces

4. Discussion

The aim of investigating a child with developmental delay is to classify brain MRI findings by trying to establish a specific diagnosis when possible with the aid of myelination milestone.

Assessment was done in 47 pediatric patients of age range (1 moths-14 years), they were 27males (57.4 %), and 20 females (42.6 %).

The proportion of children of having abnormal MRI study was 21out of 47; thus neuroimaging provided information in about (44.7%) of children with delayed development.

Although there is no considerable difference the same presentation age and sex incidence was mentioned in the study done by Momen et al, [11].

Similar yield of MRI has been reported by Momen et al., [11], and Pandey et al., [43]. Who had a yield of 58.6 % and 63% respectively and different yield with Widjaja et al., [44] and Battaglia et al., [45] who had yield 84 % and 80.8 % respectively

Such wide range could be attributed to patient selection criteria and awareness of the investigation laboratory tests.

We have included all kids referred by pediatric outpatient clinic with developmental delay, irrespective of their clinical features and its severity, whether they were syndromic or nonsyndromic.

In this study the 21 cases with abnormal MRI were evaluated for involvement of different structures. Abnormalities of ventricles and White matter mainly the corpus callosum was most common: seen in 21.3% and 31.9 % cases respectively. Widjaja et al., [44] studied 90 such children and found that Ventricles (48 %) and Corpus callosum (44 %) were the most commonly involved structures.

According to MRI finding, we have been classified MR finding into various causes. metabolic/degenerative 4.3 %, congenital and developmental 6.4 %, traumatic/neurovascular 10.6%, nonspecific 23.4%, normal 59.6 %. Althaf et al., [46] MR classification categories were as the following normal study 32%, traumatic/neurovascular diseases 31 % and congenital and developmental 17 %.

Delayed myelination milestone was noticed to form about 66.7% in infant below one year, 2/3 of this 66.7 %, were females.

It was demonstrated that about 8.5 % of total number of the patients presented with delayed development and seizures while patients presented with delayed development and autism shows 0 % delayed milestones.

The application of neuroimaging in the children with developmental delay is useful in providing valuable information regarding an etiological base for this delay; this will greatly help the clinician in counseling the concerned family and enables the couple to comprehend these information in order to help them have their own decision regarding their future reproductive choices.

The positive results help the families to understand that there were some physical factors in the brain beyond their control that accounted for this lifelong problem and help them to accept the situation better and stop their efforts for diagnosis and pay more attention for training and rehabilitation.

5. Conclusions and Recommendations

5.1. Conclusions

MRI is an important investigation in patient without a known cause of delayed milestones after clinical examination and relevant lab text, in order to establish a possible clue to the cause of developmental delay as MRI provide comprehensive evaluation of brain in children with developmental delay.

The most common MRI finding was congenital /developmentals, we found that the much more presentation was developmental delay with seizures, and much were infant less than one year, no obvious relation between MRI finding and gender is seen.

5.2. Recommendations

MRI should be performed early for all children who have developmental delay for proper diagnosis of the cause and for prognostic implications.

List of Abbreviations

CSF: Cerebrospinal fluid
DD: Developmental delay
DWI: Diffusion-weighted imaging
FLAIR: Fluid Attenuation Inversion Recovery
FOV: Field Of View
MPS: Mucopolysaccharidoses
MRI: Magnetic Resonance Imaging
PUK: Phenylketonuria
STIR: Short Inversion Recovery Time
TE: Time Echo.
TR: Time Recovery

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