DOI: https://doi.org/10.53350/pjmhs202317310

ORIGINAL ARTICLE

Prevalence and Pattern of Hypoxic Ischemic Encephalopathy on Magnetic Resonance Imaging among Pediatric patients at a Tertiary Hospital in Pakistan

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ABSTRACT

Background: Hypoxic Ischemic Encephalopathy is a frequently encountered occurrence in a pediatric setting and more prevalent in the low middle income countries. Magnetic resonance imaging (MRI) is considered a reliable source of investigation. Our study determined the imaging findings and cause of Hypoxic ischemic encephalopathy in children referred for MR Imaging to our radiology department.

Study design: A prospective cross-sectional study.

Place and duration of study: Our prospective cross-sectional study was conducted at a pediatric tertiarycare hospital, of Karachi Pakistan from 1st November 2021 to 30th October 2022.

Methods: Our study included children from newborns to 16 years of age who either had a history of fits, abnormal APGAR score, delayed cry or delayed milestones. The brain MRI was performed on 1.5 tesla scanner with a standard protocol and interpreted by Experienced Radiologists Findings were recorded on anExcel Sheet and data was analyzed on SPSS version 26. Our study included children from newborns to 16 years of age who were at risk of hypoxic insult and were born to mothers who had hypertension, diabetes milletus, history of maternal substance abuse and maternal history of fits history of fits and children who had a history of fits, abnormal APGAR score, delayed cry and/or delayed milestones. Children who were born via instrumental delivery were excluded from our study.

Result: A total number of 187 patients were included in our study with 98 males and 89 females. The most common age group involved was from age >1 year to 5 years (50.3%). The most common presenting complaints included delayed milestones (63.6%) and fits (59.9%), delayed cry (52.4). On examination 42.2% had microcephaly. One-third of the patients had a positive maternal history for diabetes mellitus, hypertension and anemia. APGAR score was checked at 1 minute and 5 minute which showed the most common APGAR score of 3-6 which was seen in 81.8% of the patients. On MR Imaging 54.5% had periventricular leukomalacia, 35.3% had deep gray matter involvement, 3.7% had germinal matrix hemorrhage, and only 1.6% had watershed infarcts. A statically significant association was seen between gestation at birth and periventricular leukomalacia (P=<0.5).

Conclusion: Hypoxic Ischemic Encephalopathy is a common occurrence in our society and MRI is the recommended modality due to its sensitivity and superior soft-tissue resolution. In developing countries due to a lack of proper facilities and awareness, there is an increased incidence of HIE which leads to increased morbidity therefore increasing awareness and early diagnosis is of utmost importance.

Keywords: Hypoxic ischemic encephalopathy, Magnetic Resonance Imaging, Pediatric population

INTRODUCTION

A common cause of cerebral palsy in children is neonatal hypoxic encephalopathy. It is a common occurrence in children with a reported rate of 1.5/1000 live births in developed countries while low-middle income countries reporting a much higher prevalence ranging from 10-20 cases per 1000 live births[1,2]. The main causative factor for neonatal HIE is asphyxia in utero or immediately after birth. Inadequate oxygen supply causes diffuse neuronal region that leads to severe global deficits. There are multiple patterns of brain injury that can result from HIE depending on the duration and severity of hypoxia and gestational age at which the child was born and can range from focal deficits to global brain injury with varying deficits[3]. Multiple neuroimaging modalities are used to diagnose the location and severity of the brain injury. Characterization of the extent of injury can be done via multiple modalities ranging from conventional ultrasound, computed tomography (CT) Magnetic resonance imaging (MRI) to newer techniques including Diffusion weighted imaging (DWI) and magnetic resonance spectroscopy (MRS)[4,5]. The clinical manifestation of HIE can vary from patient to patient. HIE has no definitive treatment and patient are mainly given supportive management in addition to treatment of the underlying cause. The main prognostic factors for long term survival include gestation at which the infant was delivered, pattern of brain injury, duration of hypoxia, and neuroimaging findings[6].

Received on 11-10-2022
Accepted on 25-02-2023

The main aim of our study is to evaluate the various consequences of hypoxic ischemic insult on MRI imaging and their various patterns of presentation and prevalence of HIE in preterm and term infants in our tertiary care setup.

METHODOLOGY

This descriptive, prospective cross-sectional study was conducted at National Institute of Child Health by Department of Radiology. The prospective data was collected from within the department dated from 1st November 2021 to 30th October 2022 through hospital records. Our study included children from newborns to 16 years of age who were at risk of hypoxic insult and were born to mothers who had hypertension, diabetes milletus, history of maternal substance abuse and maternal history of fits history of fits and children who had a history of fits, abnormal APGAR score, delayed cry and/or delayed milestones and underwent MRI at our department in the selected time frame were considered eligible to be included in our study whereas patientsdiagnosed at any other center but receiving treatment in our setup were excluded, patients who were born by instrumental deliver (vacuum assisted or forceps delivery) or malpresentation, cord prolapse and mothers with meconium stained amniotic fluid were excluded from the study. A proforma with details of hypoxic ischemic encephalopathy imaging features was filled out by investigators through patient records.

The MRI brain was performed on 1.5 T MRI scanner Toshiba, Canon with standard protocol including Axial T1 weighted Image (T1W), T2 weighted Images (T2W), Coronal Fluid Attenuated Inversion Recovery (FLAIR), Diffusion-Weighted

Imaging (DWI), Apparent diffusion-weighted coefficient (ADC) and Susceptibility-Weighted imaging (SWI). Hypoxic Ischemic Encephalopathy (HIE) was diagnosed when there was periventricular leukomalacia, deep gray matter involvement watershed infarcts and/or germinal matrix hemorrhage. Data was then analyzed in the software SPSS 26 created by the IBM.

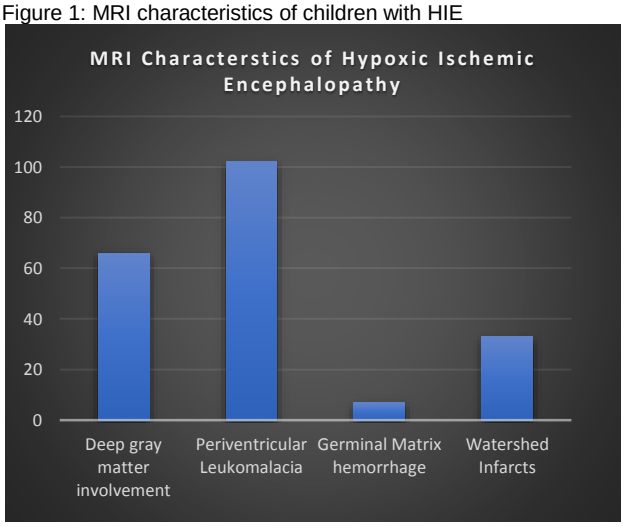
RESULTS

A total number of 187 patients were reported in our department during the study period. In our analysis we found that most patients reported were from age >1 year to 5 years (50.3%) (Table 1).

Table 1: Characteristics of children presenting with Hypoxic Ischemic Encephalopathy

Characteristics	Frequency (n) (%)
Age	1 day to 1 month: 13 (7) >1 month to 1 year: 53 (28.3) >1 year to 5 years: 94 (50.3) >5 years: 27(14.4%)
Gender	M:98(52.4) F:89(47.6)
Gestation at birth	Preterm: 96 (51.3) Term: 90 (48.1) Post term: 1 (0.5)
Positive maternal history for DM/Anemia/HTN	Yes: 126 (67.3) No: 61 (32.7)
APGAR score at birth	0-3: 3 (1.6) 4-6: 153 (81.8) 7-10: 31 (16.6)
Hypotonia/Hyporeflexia	Yes: 97 (51.8) No: 90 (48.1)
Delayed cry	Yes: 119 (63.6) No: (36.4)
Delayed milestones	Yes: 32 (17.1) No: 147 (78.6) Regression: 8 (4.3)
Fits	Yes: 112 (59.9) No: 75 (40.1)
Microcephaly	Yes: 79 (42.2) No: 105 (56.1) Macrocephaly: 3 (1.6)
Family History	Yes:2 (1.1) No:185 (98.9)
Consagenous marriage	Yes: 8(4.3) No: 179 (95.7)

Figure 1: MRI characteristics of children with HIE



The most common presenting complaints included delayed milestones (63.6%) and fits (59.9%), delayed cry (52.4). On examination 42.2% had microcephaly while only 3 patients reported macrocephaly. One-third of thepatients had a positive maternal history for diabetes milletus, hypertension and anemia. APGAR score was checked at 1 minute and 5 minute which showed the most common APGAR score of 3-6 which was seen in 81.8% of the patients while only 1.6% of the patients had an APGAR of 1-3.51.8% patients had hypotonia and hyporeflexia at presentation. Family history of HIE was seen in only 2 of the participants and while history of consanguineous marriage was seen in 4.3% of the patients (Table 1). On MRI, 54.5% had peri ventricular leukomalacia, 35.3% had deep gray matter involvement, 3.7% had germinal matrix hemorrhage and only 17.6% had watershed infarcts (Figure 1). Chi square test showed statistically significant association between periventricular leukomalacia on MRI with gestation at birth (p-value = 0.00). There was no statistically significant relation between other MRI findings including watershed infarcts, germinal matrix hemorrhage and deep gray matter involvement.

DISCUSSION

Hypoxic Ischemic Encephalopathy (HIE) is a common occurrence in the pediatric age group with a high prevalence in low to middle income countries therefore it is important to highlight the causes and findings of HIE as limited data is available discussing the presentation of HIE with respect to our clinical setup.

There are multiple risk factors for the development of HIE. Our study showed positive maternal history for Diabetes Miletus, hypertension and anemia and low APGAR score at birth are important risk factors for development of HIE. A previous study conducted in China showed similar results with HIE being more prevalent in children with intrauterine distress, low APGAR score, low birth weight and pre term birth. Low birth weight has also been commonly associated with severe HIE[7]. Immediate asphyxia is the most common cause of HIE in neonates[8]. Prolonged asphyxia causes hypoxia that leads to decreased cerebral perfusion resulting in increased lactate levels in brain and reduced ATP production. This in turns leads minimal free radical clearance causing brain injury at cellular level. HIE can lead to complex cellular and molecular changes that if not treated timely can result in permanent brain injury, therefore the timing and duration of injury is important and early treatment within the first 60 minutescan lead to reduced severity of brain injury with improved prognosis[9]. A common cause of neonatal hypoxia seen in our study was positive maternal history for comorbid diseases such as hypertension and diabetes mellitus. This can be explained by uteroplacental insufficiency causing impaired oxygenation in fetus.

The clinical manifestation used for the diagnosis of HIE can vary from mild tosevere. Altered level of consciousness with respiratory distress, reduced power and tone of muscles and seizures are important manifestations of HIE[6]. The most common manifestations in our presenting population were altered APGAR score, hypotonia, hyporeflexia, delayed milestones, fits and delayed cry. A previous study conducted in Pakistan also showed that diminished reflexes and hypotonia were common presenting neurological symptoms in their study population[10]. Children with mild HIE can present with hyperactivity, brisk reflexes, increased muscle tone with irritability or transient difficulties in feeding that typically resolves within 24 hours with and no long-term sequala. Severe HIE presents with more alarming symptoms such as lethargy, hypotonia, hyporeflexia or even apnea in severe casesand can lead to permanent brain damage. Generalized seizures is another important finding in children with severe HIE and was seen in 59.9% of our study participants. Another study conducted in Iran showed that seizure was a common presenting sign in their population[11]. Seizures can be initially refractory to standard treatment protocols. If not treated timely, severe HIE can lead to coma with additional requirement of ventilatory support[12].

The diagnosis of HIE can be made through clinical manifestation, ABG (Arterial Blood gases) and cord blood analysis[13]. This can be attributed to the fact that low APGAR score is commonly a result on intrauterine distress that subsequently

leading to hypoxia and acidosis which can be manifested in cord blood. In our study APGAR score most commonly seen ranged from 3-6 which is considered moderately low. Additionally, progression and staging of HIE can be evaluated trough different biomarkers. MRI is an important staging tool for HIE and can be used to confirm the degree of severity and evaluation of neurodevelopmental outcomes. Previously, literature has shown the involvement of posterior limb of internal capsule has a great importance in evaluating the prognosis. Additionally, the timing of MRI is also important because progressive changes take place after the initial insult[14,15,16]. The severity of the injury can be classified based on the MRI findings. In preterm infants MRI findings that show mild to moderate degree of HIE include germinal matrix hemorrhage and periventricular leukomalacia while in term infants it is confirmed by para sagittal watershed infarcts. Periventricular leukomalacia was another significant finding in preterm participants of our study. Severe HIE findings include deep gray matter and periRolandic infarcts[17]. The frequency of watershed infarct and deep gray matter lesionin our study was quite similar to a pervious study conducted; however white matter lesion manifested by periventricular leukomalacia in our population were much more common[12]. Germinal matrix was seen in only a minority of our patients which is quite similar to the previously reported literature[1]. Another method to verify severity of HIE is analysis of the umbilical cord blood for metabolic acidosis. It has been considered as a diagnostic tool worldwide however due to limited resources it is not frequently performed in our setup[19].

Treatment of HIE is dependent on symptoms. There is a general consensus that therapeutic hypothermia has been very helpful in HIE treatment, however data has shown that it is less effective in children suffering from severe HIE [20,21]. Treatment of severe HIE can include fluid and electrolyte replacement, seizure control and ventilator supportive patients presents with apnea or altered GCS[22].

CONCLUSION

Hypoxic Ischemic Encephalopathy is a common occurrence in our setup. MRI is the modality of choice for evaluating hypoxic ischemic encephalopathy detection, grading and pattern of involvement therefore it should be the modality of choice in all patients with suspected HIE and/or risk factors of HIE.

Conflict of interest: Nothing to declare

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