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EXPLORING THE CLINICAL AND ETIOLOGICAL SPECTRUM OF INFANTILE SPASMS: A COMPREHENSIVE STUDY

Paediatric Medicine

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ABSTRACT

Background: Infantile spasm (IS) is a severe epilepsy disorder that primarily affects infants and young children, often occurring in combination with West syndrome. It is considered a true Epileptic Encephalopathy and was first described by West in 1841. IS is characterized by sudden, symmetric flexion and/or extension of the body, and it can involve both flexor and extensor spasms. The incidence of IS is rare, affecting approximately 1.6 to 4.5 per 10,000 live births annually, with an average age of onset between 3 and 7 months. The gender distribution of IS shows conflicting results, with some studies suggesting a slightly higher prevalence in males. **Methods:** The study aimed to investigate the clinical and etiological aspects of infantile spasms in a tertiary care center. The goal was to facilitate early diagnosis and determine if there are preventable causes for IS. The study utilized a retrospective analysis of patient data to examine the clinico-etiological spectrum of IS. **Results:** The incidence of IS is rare, and the age of onset varies from the first week of life to 4.5 years. Various underlying causes contribute to the development of IS, including neurocutaneous syndromes, metabolic disorders, cortical malformations, perinatal brain injuries, postnatal infections, head trauma, and genetic defects. The pathophysiology of IS is still not fully understood, with theories suggesting nonspecific insults during critical brain development or abnormalities in the hypothalamic-pituitary-adrenal axis. **Conclusion:** In resource limited coutntries like India, we can reduce the burden of IS and it's treatment expences by reducing its own incidence by discovering of its causes which are mainly preventable causess like Perinatal asphyxia and hypoglycemia. So we can decrease in incidence of IS by indirectly reducing in these causes.Infantile spasms require prompt diagnosis and treatment. Hormonal therapy with corticotropin, ACTH, or steroids is the first-line treatment option. Surgical options may be considered for refractory cases with structural abnormalities or neurodevelopmental regression. Early diagnosis and treatment are associated with better treatment response and improved developmental outcomes. However, the diagnosis and treatment of IS are often delayed, and the impact of etiology on treatment outcomes requires further research.

KEYWORDS

Infantile spasm, West syndrome, epilepsy.

INTRODUCTION

Infantile spasm (IS) is a severe epilepsy disorder that occurs in infancy and early childhood. It is considered a true Epileptic Encephalopathy and can present as infantile spasms alone or in combination with West syndrome. West syndrome is characterized by cognitive decline, along with infantile spasms and specific EEG patterns known as hypsarrhythmia or modified hypsarrhythmia. The condition was first described by West in 1841 when he observed the seizures in his own son. Most cases of IS involve both flexor and extensor spasms, although either type can occur independently.[1]

The incidence of IS is rare, affecting approximately 1.6 to 4.5 per 10,000 live births, which translates to around 2000 to 2500 new cases annually. The onset of IS can range from the first week of life up to 4.5 years, with the average age of onset being between 3 and 7 months. Studies on the gender distribution of IS have shown conflicting results, with some suggesting a slightly higher prevalence in males (60:40 ratio) compared to females.[2]

IS can have various underlying causes, including neurocutaneous syndromes, metabolic disorders, cortical malformations, perinatal brain injuries, postnatal infections, and head trauma. Common associations with infantile spasms include hypoxic-ischemic insult, tuberous sclerosis, and cortical malformations. Genetic defects have also been identified as a major cause of IS.[3]

The pathophysiology of IS is still not fully understood, but two theories have been proposed. One theory suggests that IS arises from a nonspecific insult during critical brain development. Another theory proposes that abnormalities in the hypothalamic-pituitary-adrenal axis, due to immunologic dysfunction or early developmental stress, may contribute to the development of IS. Clinically, IS is characterized by sudden, symmetric flexion and/or extension of the neck, trunk, and extremities.[4] It can be classified into symptomatic and cryptogenic types, with an additional subgroup called idiopathic infantile spasm. The ictal electroencephalogram (EEG) typically shows high amplitude slow waves with brief spindle-like fast activity. A characteristic feature of clinical epileptic spasms is the rhomboid-shape appearance on surface electromyography (EMG) of the deltoids. Although certain epilepsy syndromes exhibit classic EEG patterns such as burst suppression or hypsarrhythmia, patients with epileptic spasms may display periodic and focal patterns, including hemispheric hypsarrhythmia or the absence of hypsarrhythmia on EEG.[5]

Treatment for infantile spasms should be initiated promptly upon suspicion, using hormonal therapy, antiseizure medications, or dietary changes. Hormonal therapy with corticotropin, ACTH, or steroids is the first-line treatment. In cases of refractory IS and the presence of focal-cortical structural abnormalities or neurodevelopmental regression, surgical options may be considered. Early diagnosis and treatment have been associated with better treatment response and improved developmental outcomes.[6] However, diagnosis and treatment of IS are often delayed, both in developed and developing countries, despite the characteristic EEG pattern.[7] Limited large-scale studies have explored the impact of etiology on treatment outcomes, although recent research challenges the notion that the genetic/unknown group has a more favorable outcome.[8]

Given the scarcity of research on the clinico-etiological spectrum of infantile spasms, this study aimed to investigate the clinical and etiological aspects of the condition in a tertiary care center. The goal was to facilitate early diagnosis and determine if there are preventable causes for IS.[9]

MATERIALS AND METHODS

Study Location – The study was conducted in Department of Pediatrics, S.M.S medical college and attached group of hospitals, Jaipur.
Study Design – Hospital based cross sectional study.
Study Duration – June 2021 to Dec 2022(over the course of one year) or till completion of sample size

Sample Size

Sample size was calculated at 95% confidence level, alpha error 0.05 expecting 10.6% neonatal sepsis/ meningitis as one of the etiology of infantile spasm.At 7% allowable error the required sample size was 78 cases of infantile spasm. This sample size was large enough to include varies etiologies of infantile spasm

Study Population
All children aged 3 months to 5 years who had diagnosed as Infantile Spasms in our centre

ELIGIBILITY CRITERIA
Inclusion Criteria:
The study subject fulfill the following criteria:
1. 3 months to 5-year-old diagnosed case of Infantile Spasms on the basic of history of spasms or witnessed by Pediatrician, EEG Pattern of classical or modified hypsarrthymia documented any time.
2. Those who give informed consent.

Exclusion Criteria
1. Patients who are refusing to give consent.
2. Non-Availability of care giver at time of enrolment
3. Non-Availability of Significant data or Records

Sampling Technique
A convenient sampling technique was used to enrolled the patients in study till the sample size completion and 78 patients were selected for the study.

METHODOLOGY
All children 3 months to 5 year of age who had diagnosed as Infantile Spasms were included after applying inclusion and exclusion criteria the informed consent was taken then the following data was extracted from direct interview with care giver and or record analysis.

RESULTS

Table 1 : Distribution Of Participants According To Aetiology

Aetiology	Frequency	Percent
Perinatal asphyxia	30	38.5
Hypoglycaemia	15	19.2
Brain malformations	13	16.7
NNJ	9	11.5
CNS infections	9	11.5
Cryptogenic	7	9.0
Proven genetic disease	2	2.6
Trauma	2	2.6
Cerebrovascular disease	2	2.6
Vit-B-12 deficiency	2	2.6
PKU	1	1.3

In our study, the most common causes of infantile spasms were perinatal asphyxia in 30 (38.5%) participants and hypoglycemia in 15 (19.2%) participants. Genetic diseases accounted for 2 (2.6%) cases, with one being Down syndrome and the other PKU. Additionally, 3 (3.9%) patients had metabolic diseases, including 2 with vitamin B-12 deficiency and 1 with PKU.

Table 2 : Distribution Of Participants According To Type Of Spasm

Spasm	Frequency	Percent
Flexor	53	67.9
Mixed	25	32.1
Total	78	100.0

In our study, out of the 78 participants, 53 had flexor type of spasm and 25 had mixed type of spasm.

DISCUSSION
Infantile spasms are a specific type of epilepsy disorder that mainly occurs in early childhood and can have severe neurological consequences if not treated. The disorder is often considered an age-dependent manifestation of brain damage and is characterized by a specific electroencephalography (EEG) pattern called hypsarrhythmia. It is commonly associated with neurodevelopmental regression. Infantile spasms can occur alone or in combination with a condition known as West syndrome, which is characterized by spasms, abnormal EEG patterns, and mental retardation.[10]

The diagnosis of infantile spasms relies on factors such as the patient's medical history, age, seizure characteristics, and the distinct EEG pattern. The typical onset of spasms in early childhood suggests that an immature central nervous system may contribute to the development of the disorder. The brain-adrenal axis has also been proposed as a potential mechanism, where stressors lead to excessive secretion of corticotropin-releasing hormone (CRH) in the immature brain, resulting in spasms. The clinical response to treatments such as adrenocorticotropic hormone (ACTH) and glucocorticoids can be explained by their suppression of CRH.[11]

A recent study conducted in the Department of Pediatric Medicine at SMS Medical College and Attached Hospitals Group in Jaipur aimed to investigate the clinical and etiological spectrum of infantile spasms. The study included 78 children between 3 months and 5 years of age who had been diagnosed with infantile spasms.[12]

The study participants had a mean age of 19.8 months, with a majority (41%) being younger than one year. Of the participants, 75.6% were male and 24.4% were female, while 70.5% came from rural areas and 29.5% from urban areas. Most of the children (89.7%) were born at full term, and the mean birth weight was 2.5 kg. The majority (91%) were delivered by normal vaginal delivery, and 60.3% had a history of neonatal intensive care unit (NICU) admission.

The mean age of onset for infantile spasms in the study was 8.0 months, with a range of presentation between 3 and 36 months. Similar studies have reported comparable findings regarding the age of onset and the male-to-female ratio. Some studies also highlighted the association between delayed cry at birth and the development of infantile spasms.[13] The etiological spectrum of infantile spasms can be classified into symptomatic and cryptogenic forms. In this study, 91% of the cases were symptomatic, while 9% were cryptogenic. Perinatal asphyxia was identified as the most common cause of symptomatic infantile spasms, followed by hypoglycemia. Genetic and metabolic diseases were also identified as etiological factors in a small percentage of cases.[14]

Abnormalities observed in CT/MRI scans of the participants included cystic encephalomalacia, parietooccipital gliosis, and subependymal nodules. EEG findings showed that most of the participants had either hypsarrhythmia or modified hypsarrhythmia.[15] Other studies on infantile spasms have reported similar findings regarding the etiology, including perinatal causes such as birth asphyxia, neonatal sepsis/meningitis, and hypoxic-ischemic encephalopathy. The availability of diagnostic facilities and variations in population and settings may contribute to some differences observed among studies.[16]

CT/MRI scans revealed various abnormalities, including cystic encephalomalacia, parietooccipital gliosis, and subependymal nodules. Other findings included periventricular leukomalacia, cerebral atrophy, gliosis, infarction, agenesis of the corpus callosum, and structural abnormalities such as lissencephaly and porencephaly. These imaging results support the understanding that infantile spasms often have underlying structural or metabolic abnormalities.[17]

Several previous studies have reported similar findings regarding the clinical presentation and etiology of infantile spasms. They have identified perinatal causes, genetic factors, and structural abnormalities as common underlying factors. The studies also highlight the importance of early diagnosis and effective treatment in improving outcomes for infants with infantile spasms.[18]

In conclusion, this study provided valuable insights into the clinical and etiological spectrum of infantile spasms. Perinatal asphyxia was identified as the most common cause, followed by other factors such as hypoglycemia, genetic diseases, and metabolic disorders, out of which birth asphyxia and hypoglycemia were preventable causes so by decreasing in the incidence of these conditions we can decrease the IS.

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