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Original Article

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

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ABSTRACT

Objective: Infantile spasm (IS) is a severe epilepsy disorder affecting infants and young children, often presenting in conjunction with West syndrome. Recognized as a true Epileptic Encephalopathy, IS was first described by West in 1841. The disorder manifests through sudden, symmetric flexion and/or extension of the body, involving both flexor and extensor spasms. IS is relatively rare, affecting approximately 1.6 to 4.5 per 10,000 live births each year, with an onset typically between 3 and 7 mo. Studies reveal a slightly higher prevalence in males, though findings vary.

Methods: The study was conducted in Department of Pediatrics, S. M. S. Medical College, Jaipur, aimed to explore the clinical and etiological dimensions of IS. The objective was to enable early diagnosis and identify potentially preventable causes of IS. A retrospective analysis of patient data was employed to examine the clinico-etiological spectrum associated with the disorder.

Results: IS shows a rare incidence and a varied age of onset, ranging from the first week of life to 4.5 y. The development of IS is influenced by diverse etiological factors such as neurocutaneous syndromes, metabolic disorders, cortical malformations, perinatal brain injuries, postnatal infections, head trauma, and genetic anomalies. The pathophysiology of IS remains elusive, with prevailing theories suggesting either nonspecific insults during critical brain development phases or disruptions in the hypothalamic-pituitary-adrenal axis.

Conclusion: Prompt diagnosis and intervention are crucial for managing infantile spasms. Hormonal therapy using corticotropin, ACTH, or steroids represents the primary treatment approach. In cases resistant to initial treatments and where structural abnormalities or neurodevelopmental regression are evident, surgical interventions may be warranted. Early identification and treatment correlate with more favorable responses and enhanced developmental outcomes. Despite this, delays in diagnosing and treating IS persist, highlighting the need for further investigation into how etiology affects treatment efficacy.

Keywords: Infantile spasm, West syndrome, Epilepsy

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INTRODUCTION

Infantile spasm (IS) is a critical epileptic disorder that emerges during infancy and early childhood. Recognized as a genuine Epileptic Encephalopathy, IS often presents either as isolated infantile spasms or in conjunction with West syndrome. The latter condition is noted for its cognitive deterioration coupled with distinctive EEG patterns termed hypsarrhythmia or modified hypsarrhythmia. The medical community first became aware of IS in 1841 when West documented the condition after observing seizures in his son. Typically, IS manifests through a combination of flexor and extensor spasms, although it is possible for each type to occur separately [1].

IS is relatively rare, with incidence rates ranging from 1.6 to 4.5 per 10,000 live births, equating to approximately 2000 to 2500 new cases each year. The disorder typically begins between the first week of life and 4.5 y of age, with the most common onset occurring between 3 and 7 mo. Gender distribution studies have shown a slight predominance in males over females, often cited with a 60:40 ratio [2].

The origins of IS are varied, including potential causes such as neurocutaneous syndromes, metabolic disorders, cortical malformations, perinatal brain injuries, postnatal infections, and head trauma. Notably, associations have been made with conditions like hypoxic-ischemic insults, tuberous sclerosis, and genetic anomalies, pinpointing them as significant contributors to the development of IS [3].

The pathophysiological basis of IS is not entirely understood, yet two prevailing theories offer some explanation. One suggests that IS results from a nonspecific disruption during crucial brain development phases, while another implicates abnormalities in the hypothalamic-pituitary-adrenal axis, possibly triggered by immunologic dysfunctions or early developmental stress. Clinically, IS is characterized by abrupt, symmetric movements involving flexion and/or extension of the neck, trunk, and limbs. The disorder is categorized into symptomatic, cryptogenic, and an additional subgroup known as idiopathic infantile spasm. During episodes, the ictal EEG typically displays high-amplitude slow waves accompanied by brief spindle-like fast activities, and the clinical spasms often produce a rhomboid-shaped pattern on surface electromyography (EMG) of the deltoids. While some epilepsy syndromes exhibit distinct EEG patterns like burst suppression or classic hypsarrhythmia, IS may show periodic and focal variations, including hemispheric hypsarrhythmia or an absence of hypsarrhythmia altogether [4, 5].

Treatment protocols for IS emphasize rapid initiation, utilizing hormonal therapy, antiseizure medications, or dietary modifications. Hormonal treatments such as corticotropin (ACTH) or steroids serve as the primary intervention. For refractory cases of IS, particularly those associated with focal-cortical structural abnormalities or neurodevelopmental regression, surgical interventions may be considered. Early detection and therapeutic intervention are crucial, as they are often associated with more favorable treatment responses and improved developmental outcomes. However, both diagnosis and treatment tend to be delayed globally despite the characteristic EEG patterns, underscoring a persistent challenge in medical practice [6, 7].

MATERIALS AND METHODS

Study location

The study was conducted in Department of Pediatrics, S. M. S Medical College, Jaipur.

Study design

The study was structured as a hospital-based cross-sectional analysis.

Study duration

Research was carried out from May 2019 to May 2021, or until the completion of the sample size.

Sample size

The sample size calculation was based on a 95% confidence level and an alpha error of 0.05, with an expectation of 10.6% incidence of neonatal sepsis/meningitis as a possible etiology of infantile spasm. Allowing for a 7% error margin, the required sample size was determined to be 78 cases of infantile spasm, sufficient to cover various etiologies.

Study population

The study included children aged 3 mo to 5 y diagnosed with Infantile Spasms at our center.

Eligibility criteria

Inclusion criteria

1. Children aged 3 mo to 5 y diagnosed with Infantile Spasms based on the history of spasms or as witnessed by a pediatrician, with EEG patterns of classical or modified hypsarrhythmia documented at any time.

2. Cases where informed consent was provided.

Exclusion criteria

1. Patients who refused to provide consent.

2. Instances where the caregiver was unavailable at the time of enrollment.

3. Cases lacking significant data or records.

Sampling technique

A convenient sampling technique was employed to enroll patients until the required sample size of 78 was reached.

Methodology

Children aged 3 mo to 5 y diagnosed with Infantile Spasms were included after applying the inclusion and exclusion criteria. Informed consent was obtained, followed by data extraction through direct interviews with caregivers or analysis of existing records.

RESULTS

The etiological analysis of infantile spasms among the 78 participants in our study revealed perinatal asphyxia as the most prevalent cause, affecting 30 children (38.5%). Hypoglycemia was the second most common etiology, observed in 15 participants (19.2%). Other significant causes included brain malformations and neonatal jaundice (NNJ), each accounting for approximately 11.5% of cases. Cryptogenic origins were identified in 7 cases (9.0%). Less frequent causes included central nervous system (CNS) infections, proven genetic diseases such as Down syndrome and Phenylketonuria (PKU), trauma, cerebrovascular disease, and Vitamin B-12 deficiency, each presenting in fewer than 3% of cases. Regarding spasm types, 53 children (67.9%) exhibited flexor spasms, while 25 (32.1%) displayed mixed spasm types.

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 represent a significant type of epilepsy predominantly affecting early childhood and leading to severe neurological outcomes if untreated [8]. This disorder is often seen as an age-dependent outcome of brain damage, characterized by a unique electroencephalography (EEG) pattern known as hypsarrhythmia. Neurodevelopmental regression is commonly associated with this condition, especially when it occurs alongside West syndrome, presenting with spasms, abnormal EEG, and cognitive delays [9, 10].

Diagnosing infantile spasms involves assessing the patient's medical history, age, seizure characteristics, and the distinctive EEG pattern. The frequent early childhood onset of spasms suggests a role for the still-developing central nervous system in the disorder's manifestation [11, 12]. The brain-adrenal axis is hypothesized as a potential underlying mechanism, where environmental stressors may trigger an overproduction of corticotropin-releasing hormone (CRH) in the immature brain, leading to spasms. This theory supports the effectiveness of treatments like adrenocorticotropic hormone (ACTH) and glucocorticoids, believed to reduce CRH secretion [13, 14].

This comprehensive study was conducted at SMS Medical College, involving 78 children aged between 3 mo and 5 y diagnosed with infantile spasms. The average age of the study participants was 19.8 mo, with the largest group (41%) being under one year. The gender distribution was predominantly male (75.6%) compared to female (24.4%), and a significant portion of the children (70.5%) originated

from rural areas. Most children were full-term births with an average birth weight of 2.5 kg, and 91% had normal vaginal deliveries. Additionally, 60.3% of the participants had a history of neonatal intensive care unit (NICU) admission [15].

The mean age at the onset of infantile spasms was 8.0 mo, with cases presenting from as early as 3 mo to as late as 36 mo. These findings align with other studies that noted a similar age of onset and gender distribution. Further research has linked a delayed cry at birth to the development of infantile spasms.

The etiological analysis revealed that 91% of the cases were symptomatic, while 9% were cryptogenic. The leading cause among symptomatic cases was perinatal asphyxia, followed by hypoglycemia. A smaller percentage of cases were attributed to genetic and metabolic disorders [16].

Imaging studies, including CT and MRI scans, uncovered various abnormalities like cystic encephalomalacia, parietooccipital gliosis, and subependymal nodules. EEG assessments predominantly showed patterns of hypsarrhythmia or its modifications. Consistent etiological patterns, particularly perinatal issues such as birth asphyxia, neonatal sepsis/meningitis, and hypoxic-ischemic encephalopathy, were noted. Variations in diagnostic capabilities and population demographics may account for some differences in findings across studies [17].

Additional imaging revealed a spectrum of brain anomalies, including periventricular leukomalacia, cerebral atrophy, and other significant structural changes like agenesis of the corpus callosum, lissencephaly, and porencephaly. These findings further corroborate that infantile spasms frequently stem from structural or metabolic abnormalities [18].

This study underscores the prevalence of perinatal complications, genetic influences, and structural abnormalities as common underlying factors in infantile spasms. The collected data highlight the critical need for timely diagnosis and intervention to improve outcomes for affected infants.

Overall, this investigation at SMS Medical College has provided significant insights into the clinical and etiological landscape of infantile spasms, with perinatal asphyxia emerging as the predominant cause, supplemented by other factors like hypoglycemia, genetic conditions, and metabolic disorders.

CONCLUSION

This study underscores the diverse etiological spectrum associated with infantile spasms, highlighting perinatal asphyxia and hypoglycemia as the predominant causes. The distribution of spasm types further emphasizes the clinical variability of this neurological disorder. Understanding these patterns is crucial for developing targeted therapies and improving diagnostic accuracy, ultimately enhancing treatment outcomes and reducing developmental impairments in affected children. The need for ongoing research to further delineate the etiological factors and their impact on treatment efficacy remains critical.

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AUTHORS CONTRIBUTIONS

All authors have contributed equally

CONFLICT OF INTERESTS

Declared none

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