Clinical Evaluation and Outcome of Patients with Infantile Spasm

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Abstract

Background: Infantile spasm is a catastrophic infantile seizure disorder that affects children mostly in their first year of life. Proper understanding of the presenting features and diagnostic procedures are necessary for early initiation of appropriate management.

Methods: A total of 52 consecutive patients with infantile spasm from the Department of Pediatrics, Dhaka Medical College Hospital and Dhaka Shisu Hospital, Bangladesh were selected in this descriptive type of observational study from January 2016 to December 2016. Detailed history, clinical examinations, neuroimaging and EEG were performed for each of the patients and then, they were treated with ACTH and/or prednisolone. Data were recorded in a pre-structured questionnaire and outcomes of treatment were measured for statistical analysis.

Result: Most of the patients belonged to the age group of 5-9 months with male predominance. Mean age of onset of symptoms and diagnosis of the disease was 5.2±1.6 and 8.9±4.6 months respectively. 67.3% of them had symptomatic presentation and of flexor type of spasm. 50% of them had perinatal insult and the 69.2% of them had global developmental delay before the onset of spasm. Cerebral palsy and microcephaly were the most common co-morbidities. Cortical atrophy was found in 40.4% patients and was most common abnormal neuroimaging finding but only 26.9% of the patients had classic hypsarrhythmia on baseline Electroencephalography. However, with appropriate treatment, 48.1% of them had complete reduction of spasms.

Conclusion: Although infantile spasm is a rare condition, in-depth and improved clinical and imaging understanding can help healthcare providers identify and manage the patients with infantile spasm earlier resulting in reduced hazardous developmental outcomes.

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Introduction

Infantile spasm is a seizure disorder that is also known as West Syndrome. It was first described by William West in 1841.[1] This rate type of epileptic encephalopathy of early infancy occurs mostly between 3-7 months and almost 90% of them occur within the first year of life.[2] However, it may occur up to 4 years of age.[3] Incidence of infantile spasm ranges from 2 to 4.5 live births and boys have been found to be affected more than the girls.[2,4,5]

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Clinically, infantile spasm is characterized by clusters of brief muscle contractions followed by more sustained tonic phase.[2,6] It is associated with a specific EEG pattern called hypsarrhythmia.[1] Infantile spasm is usually divided intocryptogenic and symptomatic groups.[1] Various genetic and metabolic factors have been identified to cause infantile spasm. However, even with newer imaging techniques, pathophysiological basis and the range of underlying causes of infantile spasms are still poorly understood.[2,3,7]

At the same time, the ideal treatment regimen and choice of most effective drug is still controversial.[8,9] Infantile spasm is resistant to most of the ideal antiepileptic drugs and many studies advocate hormonal treatment such as adrenocorticotropin hormone (ACTH) or prednisolone as standard care options.[8,5,9,10,11] Even with treatment, the long-term prognosis of patients with infantile spasms is associated with some degree of mental retardation in most of the cases.[1]

In this current study, we described the clinical profile, neuroimaging and EEG findings and treatment outcomes of children with infantile spasm attending at BSMMU, Dhaka.

Methods

This descriptive type of observational study was conducted in the Department of Pediatrics, Dhaka Medical College Hospital (DMCH) and Child development centre, Dhaka Shisu Hospital, Bangladesh over a period of 12 months from January 2016 to December 2016.

A total of 52 consecutive patients with infantile spasm seeking treatment at the above-mentioned hospitals were included in the study. After taking informed written consent from the parents, detailed history and relevant clinical examinations of the patients were done. Based on the etiology, infantile spasm was classified as symptomatic (known etiology) or cryptogenic (unknown etiology). Then EEG was performed for each of the patients.

The patients were treated with ACTH and/or prednisolone. Patients were routinely followed up during their hospital stay and hospital outcome of the study population was recorded. Mean and standard deviation were calculated for continuous variables and proportion was calculated for categorical variables.

Prior permission for the study was taken from the Ethical Review Committee (ERC) of Dhaka Medical College and Hospital.

Results

A total of 52 children with infantile spasm were selected as study population. Demonstrates the demographic characteristics of the study population are described in Table I. Most of the patients were in the 5-9 months of age group with a slight male predominance.

Table I: Demographic characteristics of the study population

Characteristics	Number (n=52)	Percentage (%)
Age		
<5	11	21.2
5-9	27	51.9
≥10	14	26.9
Sex		
Male	30	57.7
Female	22	42.3

Table II shows that 69.2% patients had symptomatic infantile spasm while 30.8% had cryptogenic spasms. Most of them were flexor type (67.3%) and half of them (50.0%) had an insult during the perinatal period. The mean age of onset of infantile spasm was 5.2 ± 1.6 months and mean age of diagnosis was 8.9 ± 4.6 months. 69.2% had delayed developmental onset before the spasm and on neurodevelopmental assessment, 46.2% had global delay.

Table II: Spasm profile of the study population

Infantile spasm profile	Number (n=52)	Percentage (%)
Age of onset of infantile spasm (months)		5.2 ± 1.6
Mean age of diagnosis (months)		8.9 ± 4.6
Etiology		
Symptomatic	36	69.2
Cryptogenic	16	30.8
Type		
Flexor	35	67.3
Extensor	8	15.4
Mixed	9	17.3
Insult period		
Prenatal	9	17.3
Perinatal	26	50.0
None	17	32.7
Development before onset of spasm		
Normal	16	30.8
Delayed	36	69.2
Neurodevelopmental assessment		
Motor delay	11	21.2
Global delay	24	46.2
Normal	17	32.7

Almost 60% of the patients had cerebral palsy and 55.8% patients had microcephaly (Table III).

Table III. Associated co-morbidities of the study population

Associated co-morbidity	Number (n=52)	Percentage (%)
Cerebral palsy		
Yes	31	59.6
No	21	40.4
Microcephaly		
Yes	29	55.8
No	23	44.2

Study population had undergone ultrasonogram and CT scan of the brain. Neuroimaging showed that 40.4% of patients had cortical atrophy, 7.7% ventriculomegaly, 1.9% malformation, 44.2% normal and 5.8% had other findings (Figure 1).

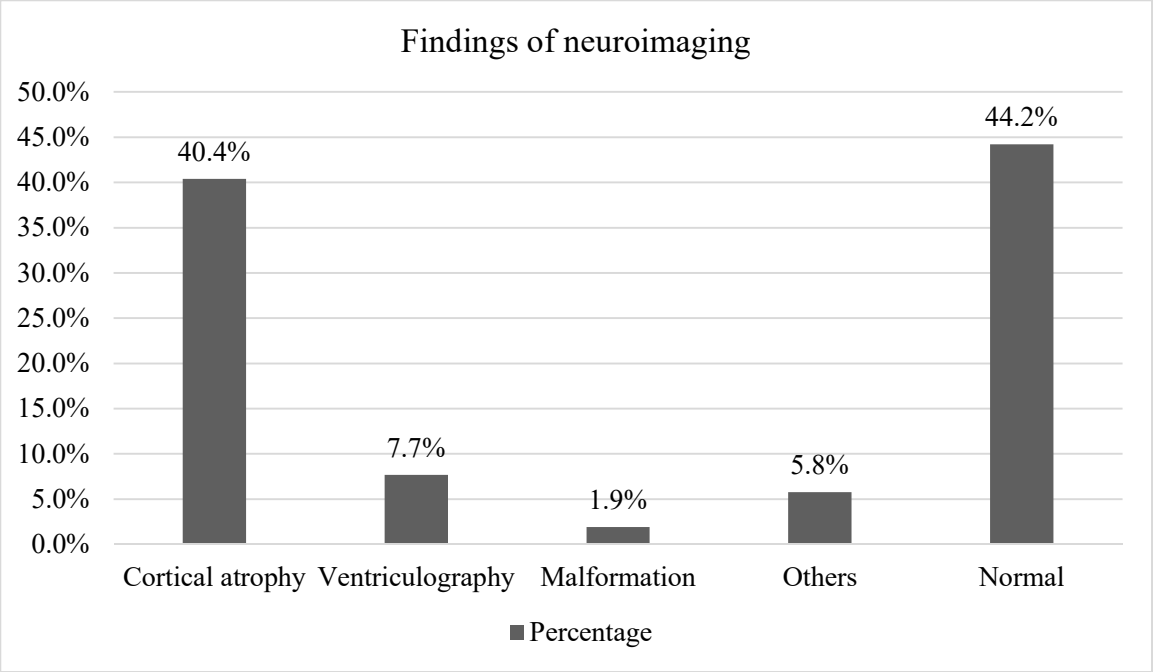

Figure 1. Neuroimaging findings of the study population

We have looked for hypsarrhythmic EEG changes on the baseline EEG. We have found 26.9% classic hypsarrhythmia, 23.1% modified hypsarrhythmia, 23.1% hypsarrhythmia with burst suppression and 26.9% patients had hypsarrhythmia with focal spike (Table IV).

Table IV: Distribution of baseline EEG findings of the study population

Baseline EEG findings	Number (n=52)	Percentage (%)
Classic hypsarrhythmia	14	26.9
Modified hypsarrhythmia	12	23.1
Hypsarrhythmia with burst suppression	12	23.1
Hypsarrhythmia with focal spike	14	26.9

Table V demonstrates the outcome measures after treatment. It shows that 48.1% of the patients had complete cessation of the spasm and 32.7% had reduction of spasm to <50% and mean time to cessation of spasm was 11.2± 2.3 days. However, 73.1% hypsarrythmia did not disappear on EEG (Table V).

Table V. Outcome measures of the study population after treatment

Baseline EEG findings	Number (n=52)	Percentage (%)
Cessation of spasm		
Complete cessation of spasm	25	48.1%
Reduction of spasm 50% or more	10	19.2%
Reduction of spasm <50%	17	32.7%
Time to cessation of spasm (days)	11.2± 2.3	
Disappearance of hypsarrythmia on EEG		
Yes	14	26.9%
No	38	73.1%

Discussion

On clinical evaluation of 52 patients, we have found that the mean age of onset of spasm of the patients was 5.2 ± 1.6 months. Study done by Sharma & Viswanathan found that the average age of onset of spasm was 7 ± 3 months.[12] However, mean age of diagnosis of our study population was 8.9 ± 4.6 months. This lag in diagnosis and initiation of treatment may be due to rarity of the disease and subsequent delay in proper treatment.[1]

We have found that the male group was predominant. Baram et al., LúðAvígsson et al. and others have also found similar dominance in their studies.[13,14,1,15,16] However, Iype et al. have found female predominance.[17]

We had found that most of the patients (69.2%) of our study had symptomatic infantile spasm. It was similar to the study done by Osborne et al.[18] but in an Indian study, they found higher percentage of symptomatic patients.[15]

More than two-thirds of them had flexor type of spasm and mixed type of spasm was the least group. Kareem et al. had found similar findings in their study.[1] Half of them had some sort of insult during their perinatal period.

More than two-third of them had delayed development before the onset of the spasm. Almost half of them had global delay on neurodevelopmental assessment. However, Kareem et al. and have found higher level of developmental delay in their studies.[1,15]

Around 60% of the patients of our study population had cerebral palsy and more than half of them had microcephaly. Kareem et al. have found that vision impairment, hearing impairment and microcephaly were the most common co-morbidities.[1]

Neuroimaging showed that more than 50% of the study population had some sort of abnormal findings and cortical atrophy was the most common abnormal feature. Apart from that, a small percentage of them had ventriculopathy, malformation and other findings of the brain.

On baseline EEG, a range of hypsarrhythmia findings such as classic hypsarrhythmia, modified hypsarrhythmia, hypsarrhythmia with burst suppression and hypsarrhythmia with focal spike were found. However, only 26.9% participants had classic hypsarrhythmia on the EEG.

After treatment, approximately half of the patients had complete cessation of the spasm and nearly one-third had a reduction of spasm to <50%. Mean time required for cessation of spasm was 11.2 days. Such favored response with steroids is documented in many other previous studies.[1,19,20]

Limitations

We did not perform detailed metabolic investigations and genetic studies in our study. Further study with detailed metabolic and genetic investigations may reveal additional clinical and pathophysiological features of the patients with infantile spasm.

Conclusion

In depth clinical profile and diagnosis course is necessary to reduce the time lag of initiation of treatment. Proper diagnosis and treatment with updated protocols can minimize the long-term consequences of infantile spasm.

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