INTRODUCTION
Infantile spasm is a unique seizure disorder that occurs almost exclusively in infants. It was first described by Dr. W. J. West in 1841 in his own son and the triad of infantile spasms, hypsarrhythmia on electroencephalogram (EEG) and mental retardation is called West syndrome. Incidence of infantile spasms is 1:4000 live births in United States and Europe and is more common in males. It accounts for 1.4-3.9% of childhood epilepsies. Peak age of onset is 4-6 months of age and 90% of infantile spasms begin before 12 months of age. It is very rare for infantile spasms to begin before one month or after 18 months of age. Clinically, attacks are characterized by a series of sudden muscular contractions in which the head is flexed, arms are extended and legs are drawn-up (flexor spasms). Other less common presentations includes head nodding, extensor spasm or rarely a brief clonic seizure.

Clinical Profile and Response to Oral Prednisolone in Infantile Spasm
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ABSTRACT
Objective: To evaluate the clinical profile and response to oral prednisolone in infantile spasms.
Study Design: Case series.
Place and Duration of Study: Neurology Department, The Children Hospital and Institute of Child Health, Multan, from July 2005 to June 2007.
Methodology: Fifty patients of infantile spasms were studied. Age, gender, age at onset of seizures, type of spasms (flexor, extensor or mixed), history of intrapartum asphyxia, developmental history, dysmorphic facial features, any hypopigmented/ hyperpigmented skin lesions, computed tomogram and electroencephalogram findings and response to oral prednisolone was noted. Data was analyzed statistically by SPSS 10. Descriptive statistics was used to find out frequencies and percentages of all above mentioned variables. Chi-square test was applied to determine the association between these variables and response to treatment. P-value of less than 0.05 was taken significant.
Results: Male to female ratio was 2.1:1. Mean age of babies was 6.5±3.35 months. Mean age at onset of seizures was 5.35±3.52 months. Flexor spasms was seen in 32 (64%), extensor spasms in 8 (16%) and mixed spasms in 10 babies (20%). Symptomatic infantile spasms were noted in 48 (96%) babies while two babies (4%) were having cryptogenic infantile spasm. History of intrapartum asphyxia was noted in 54% of symptomatic cases. Favourable response to oral prednisolone was seen in 27 babies (54%). Except male gender, none of the other variable reached the statistical significance for favourable response to treatment.
Conclusion: Infantile spasms were found more common in males, flexor spasms were the commonest type noted. Symptomatic spasm was noted in 96% of cases and intrapartum asphyxia was the commonest cause of symptomatic group. Response to oral prednisolone was noted in more than half of cases of infantile spasms.

Key words: Infantile spasms. Flexor spasms. Intrapartum asphyxia. Prednisolone.

Infantile spasms are divided in two groups, cryptogenic and symptomatic according to etiology. Cryptogenic or idiopathic group accounts for 10-15% of cases and represent the type of infantile spasms in which no apparent preceding neurological disorder is identified and infants are develop mentally appropriate for age. Symptomatic group represents 85-90% of cases and are caused by some underlying serious disorder of brain. The common causes of symptomatic group are focal cortical dysplasias, lissencephaly, unilateral megalencephaly, pachygyria, perinatal infections, birth asphyxia, neurocutaneous disorders and metabolic disorders.

Infantile spasms are accompanied by characteristic EEG findings called hypsarrhythmia (chaotic or disorganized background activity consisting of high amplitude slow waves mixed with spikes and polyspikes).

Infantile spasms are the specific type of seizure disorder which poses difficulty in diagnosis and treatment. Many studies have been done to find out the best treatment option, which is still controversial. Treatment option includes oral prednisolone, ACTH, vigabatrin and high dose pyridoxine.
This study was conducted to evaluate the clinical types of infantile spasms and response to oral prednisolone.

**METHODOLOGY**

This study was conducted at Neurology Department of Children Hospital and Institute of Child Health, Multan, from July 2005 to June 2007. Fifty babies diagnosed as infantile spasms were included in the study. These infants were referred to Neurology outpatient department for diagnosis and management.

Diagnosis of infantile spasms was made on the basis of characteristic history of flexor, extensor or mixed myoclonic jerks occurring in clusters with onset before one year of age and presence of hypsarrhythmia (chaotic or disorganized background activity consisting of high amplitude slow waves mixed with spikes and polyspikes) on EEG.

Infants having characteristic history but not accompanied by hypsarrhythmia on EEG or having other types of myoclonic epilepsies (benign familial myoclonic epilepsy of infancy, benign myoclonus of infancy) were excluded from this study.

Data was collected by a neurologist. A proforma was used to record the details of history including age at onset of seizures, gender, type of spasms (flexor, extensor or mixed), history of intrapartum asphyxia, developmental history, history of meningitis or encephalitis in neonatal or infantile period and family history of such illness.

All babies were examined for dysmorphic facial features or any hypo or hyperpigmented skin lesion. Detailed systemic and neurological examination was performed in every baby.

Fundoscopy was done for any optic atrophy or retinal changes.

Following investigations were performed: EEG in all infants for hypsarhythmia, computed tomography (CT) scan of brain was also done in all babies for evaluation of the cause of infantile spasms, while metabolic screening, TORCH titre and chromosomal analysis were performed in selected patients where history and examination was suggestive.

The study was approved by the Ethical Committee of the Institute and informed consent was also obtained from parents for the start of oral prednisolone.

Before the start of treatment babies were evaluated to find out focus of infection clinically and, if needed, investigations (complete blood count, chest X-ray and urine examination) were performed.

Oral prednisolone was started with dose of 2 mg/kg/day in three divided doses along with antacid.

Babies were monitored closely for response and side effects of prednisolone. Seizure frequency and duration was noted before and after one week of treatment for measurement of response. Response was measured after 2 weeks of treatment. Favourable response was defined as either complete cessation or at least 50% reduction of previous frequency of seizures. If favourable response was noted then prednisolone was continued for further 2 weeks and tapered over a period of another 2 weeks with total duration of 6 weeks treatment. If after 2 weeks no response was found then prednisolone was tapered and stopped in one week.

Babies were monitored for the side effects of treatment including infection (respiratory, gastrointestinal, skin or urine), hypertension and electrolyte imbalance. Blood pressure was checked daily during first week of treatment. Complete blood counts and urine examination was done if history was suggestive of infection. Electrolytes were monitored weekly.

Data was analyzed statistically by SPSS 10, to find out frequencies and percentage of different variables (age at onset of seizures, sex, type of spasms, history of intrapartum asphyxia, delayed development, CT scan and EEG findings and response of prednisolone). Association between these variables and response to treatment was determined by using the chi-square test. P-value of less than 0.05 was taken as significant.

**RESULTS**

Fifty children of infantile spasms were studied. Out of which 34 babies (68%) were males and 16 (32%) were females with ratio of 2:1: 1. Mean age of babies was 6.5±3.35 months with range of 3 months to 1.5 years. Mean age at onset of seizures was 5.35±3.52 months with range of 2 weeks to 12 months. Three babies (6%) developed seizures at less than one month of age, 38 (76%) between 1-6 months and 9 (18%) between 7-12 months of age. Flexor spasms were seen in 32 babies (64%), extensor spasms in 8 (16%) and mixed spasms in 10 babies (20%).

Symptomatic infantile spasms with delayed development were noted in 48 (96%) babies while 2 babies (4%) were having cryptogenic infantile spasm. Causes of symptomatic infantile spasms are shown in Table I. Hypsarrhythmia pattern on EEG was seen in all 50 patients (100%) in this study. CT scan was performed in all patients and results are shown in Table II.

Favourable response of prednisolone was noted in 27 (54%) patients while no response was seen in 20 (40%) infants. In 3 (6%) patients treatment was stopped after one week due to respiratory infection. All infants showed favourable response within one week of treatment.

Relapse after favourable response was noted in 4 (8%) patients in this study. Severe respiratory infection was noted in 3 babies. No other major side effect was noted in this study.
In this study, the most common type of infantile spasms were flexor spasms seen in 64% of babies. Flexor spasms were noted in 55% of patients by Cvitanovic and 34% by Rasmussen. Symptomatic infantile spasms were seen in 96% of patients in this study. The number of patients with symptomatic versus cryptogenic spasms varies considerably in different studies but symptomatic cases accounts for the vast majority of cases. Hancock and colleagues mentioned symptomatic spasms in 66% of affected infants in their study. Dreifuss noted symptomatic group in 85-90% of cases. Idiopathic cases were seen in 4% in this study while it was noted between 9-14% by Matsumoto, Singer and Riikonen. Most common cause of symptomatic infantile spasms was intrapartum asphyxia, seen in 27 patients (54%) in this study. This finding does not correlates with Western studies in which neuronal migrational disorders (focal cortical dysplasias, lissencephaly, unilateral megalencephaly and pachygyria), neurocutaneous and metabolic disorders were mentioned as common causes of symptomatic group. This discrepancy may be due to the higher incidence of intrapartum asphyxia in our setup due to multiple factors. Additional reasons could be lack of referral and existence of specialized services.

In this study, favourable response to oral prednisolone was observed in 27 (54%) patients. This finding can be correlated with Nabbout study mentioning efficacy of corticosteroids in 60% of patients. However, Lombroso, Hrachovy and Snead have mentioned approximately 70% efficacy of prednisolone in their studies. This difference may be due to the presence of higher number of symptomatic group of infantile spasms in this study, which makes up to 20-25% of cases of symptomatic infantile spasms in literature.

All variables were analyzed statistically for their contribution in response to treatment and are shown in Table III. Male gender was associated with favourable response. None of the other variable reached the statistical significance for response of treatment.

**DISCUSSION**

Infantile spasms is a rare seizure disorder of the infancy. In this study, infantile spasms were seen more frequently in males. This observation is supported by Western literature, mentioning high incidence of infantile spasms in males.

Seventy six percent of babies developed seizures between 1-6 months of age in this study. This finding can also be correlated with Western literature mentioning the peak age of onset of seizures between 4-6 months in infantile spasms.

In this study, the onset of seizures in neonatal period was found in 3 babies which is an unusual age for infantile spasms. These babies were having brain malformations and responded poorly to prednisolone. Infantile spasms can rarely occur in neonatal period which poses difficulty in diagnosis and management.

### Table I: Causes of infantile spasms (n=50).

<table>
<thead>
<tr>
<th>Name of causes</th>
<th>Number of patients</th>
<th>Percentage of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intrapartum asphyxia</td>
<td>27</td>
<td>54%</td>
</tr>
<tr>
<td>Post infectious</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pyogenic meningitis</td>
<td>04</td>
<td>08%</td>
</tr>
<tr>
<td>Post TBM*</td>
<td>02</td>
<td>04%</td>
</tr>
<tr>
<td>Brain malformations</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Porencephaly</td>
<td>03</td>
<td>06%</td>
</tr>
<tr>
<td>Lissencephaly</td>
<td>02</td>
<td>04%</td>
</tr>
<tr>
<td>Pachygyria</td>
<td>01</td>
<td>02%</td>
</tr>
<tr>
<td>Congenital infections</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CMV** infection</td>
<td>02</td>
<td>04%</td>
</tr>
<tr>
<td>Down syndrome</td>
<td>02</td>
<td>04%</td>
</tr>
<tr>
<td>Post traumatic (head injury)</td>
<td>01</td>
<td>02%</td>
</tr>
<tr>
<td>No cause found</td>
<td>06</td>
<td>12%</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100%</td>
</tr>
</tbody>
</table>

* Tuberculous meningitis; ** Cytomegalovirus.

### Table II: Computed tomogram (CT) findings in infantile spasms (n=50).

<table>
<thead>
<tr>
<th>CT scan findings</th>
<th>Number of patients</th>
<th>Percentage of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral atrophy</td>
<td>33</td>
<td>66%</td>
</tr>
<tr>
<td>Porencephaly</td>
<td>03</td>
<td>06%</td>
</tr>
<tr>
<td>Lissencephaly</td>
<td>02</td>
<td>04%</td>
</tr>
<tr>
<td>Pachygyria</td>
<td>01</td>
<td>02%</td>
</tr>
<tr>
<td>Hydrocephalus</td>
<td>02</td>
<td>04%</td>
</tr>
<tr>
<td>Periventricular calcifications</td>
<td>02</td>
<td>04%</td>
</tr>
<tr>
<td>Normal</td>
<td>07</td>
<td>14%</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>100%</td>
</tr>
</tbody>
</table>

### Table III: Factors associated with response of prednisolone.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Chi-square value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (1-6 months) at onset of seizures</td>
<td>3.234</td>
<td>0.520</td>
</tr>
<tr>
<td>Male gender</td>
<td>8.522</td>
<td>0.014</td>
</tr>
<tr>
<td>Flexor spasms</td>
<td>8.825</td>
<td>0.066</td>
</tr>
<tr>
<td>Symptomatic spasms</td>
<td>1.673</td>
<td>0.432</td>
</tr>
<tr>
<td>Delayed development</td>
<td>1.775</td>
<td>0.412</td>
</tr>
</tbody>
</table>

In this study, the peak age of onset of seizures between 1-6 months of age in this study. This finding can also be correlated with Western literature mentioning the peak age of onset of seizures between 4-6 months in infantile spasms.

In this study, the onset of seizures in neonatal period was found in 3 babies which is an unusual age for infantile spasms. These babies were having brain malformations and responded poorly to prednisolone. Infantile spasms can rarely occur in neonatal period which poses difficulty in diagnosis and management.
Clinical profile and response to oral prednisolone in infantile spasm

In a recent randomized trial, large doses of prednisolone were as effective as ACTH but still there are insufficient data to recommend any treatment schedule for infantile spasms.23

Lombroso and Hrachovy found no statistical difference between ACTH and prednisolone while Sneed found ACTH more effective than prednisolone.18-20

In this study, prednisolone was used for the treatment of infantile spasms as it is easily available, economical and equally effective to ACTH as mentioned in many studies. ACTH is expensive, has more severe side effects and also have problems of availability in our setup.

Various factors were analyzed statistically for their contribution in response of treatment. Male gender was associated with favourable response. None of the other variable reached the statistical significance for response of treatment. Significance of favourable response in male gender may not be generalized due to small sample size.

CONCLUSION

Infantile spasms were found more common in males and flexor spasms were the commonest type noted. Intrapartum asphyxia was the commonest cause of symptomatic spasms in this study. Response to oral prednisolone was noted in more than half of cases of infantile spasms. As it is easily available, economical and having fewer side effects, so it can be tried in the treatment of infantile spasms.

REFERENCES