

## Study of Thirty Two Patients with Infantile Spasms Admitted to Baghdad Medical City

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### ABSTRACT:

#### BACKGROUND:

Infantile spasms is rare epileptic syndrome affect most often infants in first year of life, occur in paroxysmal attacks in clusters especially in periods of sleep transition range in number from few spasms to many up to one hundred, and associated with crying and abnormal behavior .

#### OBJECTIVES:

Study various aspects of conditioncauses, clinical features, electroencephalograms, radiological imaging, therapeutics choices, identification the variations in our patients and outcome.

#### PATIENTS AND METHODS:

the study enrolled thirty two infants referred to child welfare hospital and epilepsy clinic of Baghdad teaching hospital in medical city of Baghdad and were followed up in outpatient clinic of these hospitals for a period extend From beginning of January 2015 to end of January 2016. All data are encoded in patient file and discharging card. Study design was hospital based description of data from patients'records.

#### RESULTS:

Male-female ratio is 1:1 , age of presentation range from four to ten month,lag period between early seizures and diagnosis was range from two weeks to four months .two weeks in two cases four week in 20 cases ( 62 % ) , 10 cases present with more than four weeks delay (31.25%)seizure types were flexor spasms in 14 (43.75%) , extensor in 6 (18.75%) , and mixed in 12 patients (37.5%) , symptomatic cases were 24 (75 % ) , idiopathic in 8 (25 %).

Mode of delivery (18 patients delivered by caesarean section 56.25 % , 14 patients 43.75 % delivered by normal vaginal mode). Causes and gender relation, was that Symptomatic was more than idiopathic in both genders.

The relation of gender to etiologic types, Tuberous sclerosis was the most common etiology in female, but neonatal and other disorders was the most common etiology in male. In Response to treatment and outcome ,16 patient (50%) had Complete remission of spasms, and 15 patient (50%) end with Severe developmental delay .

#### CONCLUSION:

Flexor type is commonest clinical types. Symptomatic group is predominant etiological types, neurocutaneous syndrome is commonest cause in symptomatic group .Hypsarrhythmia is documented in majority of patients Brain atrophy is the commonest in radiological films .Steroids is main treatment. Infantile spasms had poor prognosis, in terms of neurobehavioral development.

**KEYWORDS:** epileptic spasms, hypsarrhythmia, developmental delays, ACTH.

### INTRODUCTION:

An infantile spasm (West syndrome) is the best known epilepsy syndrome of infancy. It consists of a triad of epileptic spasms, hypsarrhythmia and psychomotor regression. <sup>(1)</sup> Perhaps no other epilepsy syndrome in existence engenders more

dread among neurologists than infantile spasms. First described 171 years ago by Dr. William James West in an article in Lancet regarding his own son .<sup>(2)</sup> It has been known by many names over the years, including salaam attacks, salaam convulsions, generalized flexion epilepsy syndrome, Blitz-Nick-Salaam-Kr'ampfe, eclampsianutans , flexion spasm , infantile spastic epilepsy , jackknife convulsion syndrome , jackknife spasm , massive myoclonia syndrome , and nodding spasms .<sup>(3)</sup>

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**Patients and methods:** The study enrolled thirty two patients who were admitted to pediatrics inpatient wards and outpatient clinics of child welfare teaching hospital , in addition to patients who had followed up in epilepsy clinic in Baghdad teaching hospital. These two hospitals are tertiary health care centers, serve and produce medical care to all people live in Baghdad and governorates of Iraq republics.

Age at diagnosis range from 2 months- 2 years (all were below one year except two cases), data was collected from records of patient files and discharging cards.

History , physical examination and evaluation carried out by teams of doctors concerned by neurological disorders of children (pediatrics neurology unit in child welfare teaching hospital ) , cerebrospinal fluid testing done in about one third of patients , some related investigations such as screening tests of feto – maternal infections and neuro – metabolic disorders are not done in all patients but requested when indicated , basic metabolic tests and neuro-imaging done in medical city. Imaging reports interpreted by radiologist and all electroencephalograms (EEG) studies are interpreted by epileptologist.

Investigations include biochemistry, hematological, serological tests of mothers and their babies and tandem mass spectrometry (MS MS). All patients had C-T scan and MRI of brain. The patients are evaluated by ophthalmologist. EEG requested initially and repeated after 14 days of treatment, then every month when the child attends in out-patients clinic for follow up. Some patients are assessed by dermatologist, when they had skin lesions. Variables which are analyzed as following : age , gender, age at presentation, lag period between initial seizures and diagnosis , presence of neonatal events , types of seizures , EEG findings , causes , imaging findings , laboratory tests , treatment , response to therapy , outcome and death number . Time period of study extend from beginning of January 2015 to end of January 2016.

- Inclusion criteria : Infants present with typical spasms plus:
  - 1-EEG findings consistent with epileptiform discharges either hypsarrhythmia and its variants or others abnormalities of epileptic nature.
  - 2- Abnormal development.
- Exclusion criteria are :

Infants present with clinical spasms but normal EEG study. And, seizures other than semiology of typical epileptic spasms

Diagnosis of syndrome is by video records or by direct observation of baby in hospital , then the EEG confirm the presence of electric discharges which are consistent with this syndrome , after that , investigations are started after complete skin examination by us or by dermatologist and dysmorphology exclusion . Initially the brain images by C-T scan to detect intracranial calcifications and hemorrhages, then MRI to detect cortical dysplasia and malformations. If no skin lesions, no syndromic associations, and cortical malformations are excluded. Then we send serological tests of mothers and their infants, these include IgG, IgM immunoglobulin for toxoplasmosis, rubella, others, like herpes simplex type 1 and 2, hepatitis viruses and HIV. mass spectrometry for metabolic disease screening (msms) tests done for 10 patients.

Treatment protocols was using steroids mainly, if no response or relapse occur in spite of perfect dosing and time, then treatment change to other antiepileptic such as sodium valpoate, benzodiazepine and others Depakien syrup used in most patients who failed to response to initial steroids, the dose is starting with 10 mg per kilogram body weight per day to maintenance dose of 30 mg/ kg/ day. Clonazepam (rivotril) in about one third of cases in dose of 0.01 - 0.04 mg/kg/day, vigabatrin ( sabril ) in one patient in dose 50 mg \kg\day , increasing gradually to 150 mg \kg\day. Total duration of therapy by this drugs not exceed six month . , levetiracetam ( keppra ) , carbamazepine (tegetol) , oxcarbazepine (trileptal) , pheyntoin , Phenobarbital , Topamax and others used in some patients .

Steroids protocol which advocated in this study is depend on recommendations of international league against epilepsy

Some patients who were referred to us had already on one or more antiepileptic , and others present without treatment , we had starting our regime after assessment and clinical evaluation . firstly ACTH depot injections if failed then prednisolone syrup and if still no satisfactory response we treat by vigabatrin tablets or syrup and others .

Steroids used in 31 patients (96.9%), ACTH used in 30 (93.7%) of babies , prednisolone in 1 patient , vigabatrin in one patient . treatment protocols are 0.25 mg of ACTH depot formula daily in initial three days then

## INFANTILE SPASMS BAGHDAD

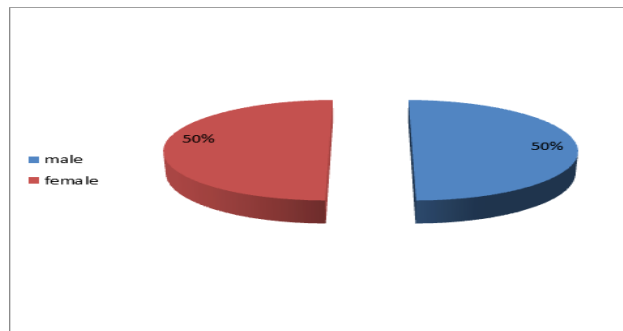
tapering over six weeks ( first two week 0.25 mg on alternate day ,second two week 0.25 mg every three days then the last two week 0.25 mg every four days ) and complete regimens by using prednisolone syrup 15 mg per 5 cc , ( 2mg per Kg. over 2 weeks then tapering over six weeks ) , total duration of steroid treatment is 14 weeks . prednisolone regimen is eight weeks duration ,in first two weeks, the dose is 2 mg per kg twice or thrice daily , then one mg per kg per day for two weeks , and the drugs is tapered over four to six week .

Follow up of treated patients was by clinical cessation of spasms and EEG. assessment and re-evaluation are taken up every month regularly in out – patient clinics , include clinical examination , weight measuring , serum electrolyte , follow up extend from six month to one year . Also follow up of the cases is accomplished by telephone mobile. All data which extracted from patients files are copied in photo format and kept it in my computer.

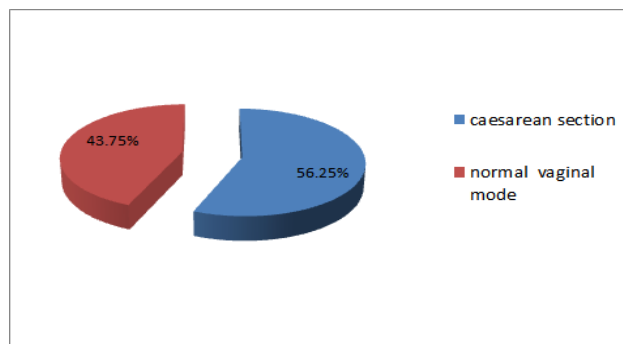
Statistical manipulations of data are accomplished by using software of Microsoft office version 2010 and excel application. The P value calculated by using chi Square test, it was considered significant if  $<0.05$ .

### RESULTS:

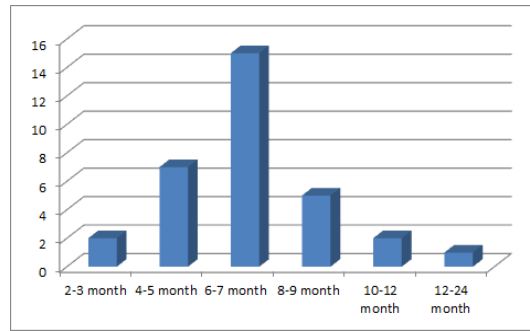
Death occurred in eight patients, aged from 4 to 38 months; the mean age at death was 20 months. Follow-up for the 20 survivors ranged from 23 to 88 months after initial diagnosis of IS: the mean duration of follow-up for survivors was 55 months. Of the eight deaths, only one was related to treatment (sepsis while on ACTH); the others died from their underlying disease. Only two infants (7%) had mild non-handicapping conditions: well-controlled seizures in one, and monoparesis in the other. None of the children was neurologically normal at the conclusion of the follow-up period. Other result is shown in the following tables:



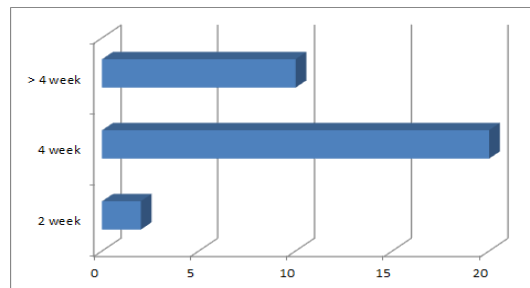
**Fig. 1: Gender frequency (Sixteen patients were male 50 %, 50% were female male to female ratio 1: 1).**



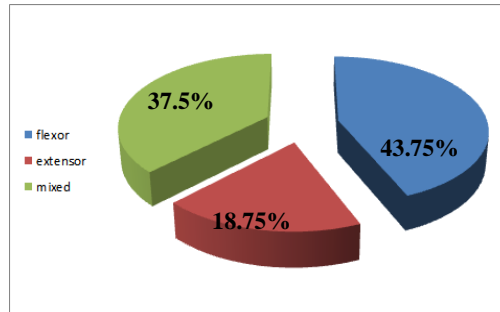
**Fig. 2 :Mode of delivery (18 patients delivered by caesarean section 56.25 %, 14 patients 43.75 % delivered by normal vaginal mode).**



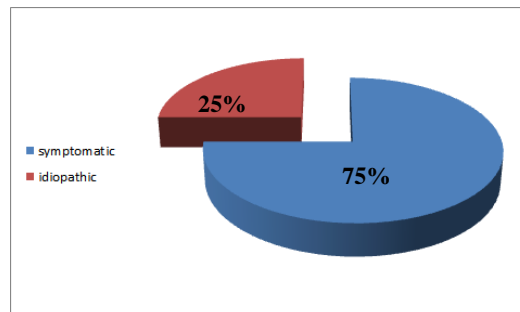
**Fig.3: Age incidence (The age range of patients were from two month to two years with peak age of incidence from 4 months- 10 months are 27 ( 84.3 % ) of patients, P value =0.025)**



**Fig. 4: Lag period between early seizures and diagnosis ( Lag period between early seizures and diagnosis was range from two weeks to four months .two weeks in two cases four week in 20 cases ( 62 % ) , 10 cases present with more than four weeks delay (31.25%).**



**Fig. 5: Clinical types of seizures: flexor 14 (43.75 %), extensor 6 (18.75%), mixed 12 (37.5%)**



**Fig. 6: Etiologic types: symptomatic 24 (75%), idiopathic 8 (25%).**

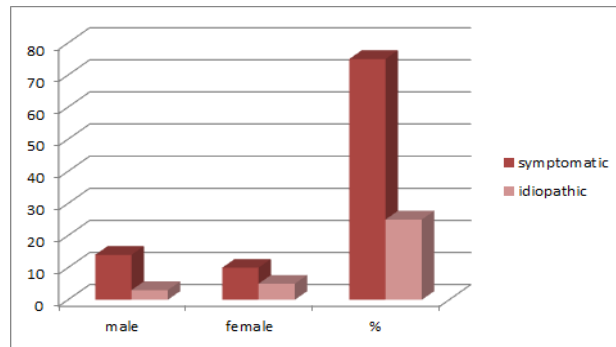


Fig.7 :Causes and gender relation, chi sq. = 0.126423, P value 0.0470  
Symptomatic was more than idiopathic in both gender.

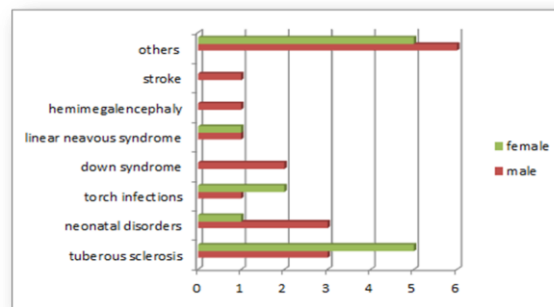


Fig. 8 :Relation of gender to etiologic types, P value =0.037  
Tuberous sclerosis was the most common etiology in female, but neonatal and other disorders was the most common etiology in male.

Table 1 : Response to treatment, outcome and adverse reactions of drugs.

| Item                              | No. | %     |
|-----------------------------------|-----|-------|
| Complete remission of spasms      | 16  | 50    |
| Partial response                  | 12  | 37.5  |
| No response                       | 2   | 6.25  |
| Outcome                           |     |       |
| Evolving to intractable seizures  | 6   | 18.75 |
| Spastic quadriplegia              | 4   | 12.5  |
| Haemiparesis                      | 2   | 6.25  |
| Severe developmental delay        | 16  | 50    |
| Mild- moderate mental retardation | 4   | 12.5  |
| Drugs adverse reactions           |     |       |
| Vomiting                          | 3   | 9.38  |
| Feeding problems                  | 4   | 12.5  |
| Obesity and over weight           | 10  | 31.25 |
| Skin rash                         | 2   | 6.25  |

In Response to treatment and outcome, 16 patients (50%) had complete remission of spasms, and 15 patient (50%) ends with severe developmental delay

**DISCUSSION:**

Male to female ratio 1:1, in studies carried out in both developing and developed countries where male slightly predominate. (Taghdiri et al.2013)<sup>4</sup> studies in Islamic republic of Iran ,

were male slightly predominate , study of (Wael H 2011)<sup>5</sup> in Amman (Jordan) male predominate 74% , study of (Amira M , Shourouk W 2014)<sup>6</sup> also in Jordan were 60% male 40% female , study of (Kenton R et al. 1997)<sup>7</sup> carried out in south Carolina , USA included total of 28 \ infants , 18 64% , are male , 10 36% are female , study of (Riikonen RS 2010)<sup>8</sup> in Finland male were slightly predominate . The role of gender in causes and outcome of infantile spasms is poorly correlate as most studies state this.

Initial presentation at early months as in (Kenton R H et al.1997)<sup>7</sup>, presentation range from 1 – 13 month. The study of (mahjoob N al naddawi 2008)<sup>9</sup> he report 80% of cases present from 2-10 month.

Clinical types of cases presented as flexor spasms were 14 (43.75%) , extensor in 6 (18.75%) , and mixed in 12 patients (37.5%) . these percentages are same in some studies but differ with some as in studies of (Riikonen R S1982)<sup>10</sup> he had found commonest type was mixed , and (Mahjoob N al naddawi 2008)<sup>9</sup> report 45.5% flexor spasms . study of (Virginia wong 2001 )<sup>11</sup> in hong Kong she found

The percentage of symptomatic and idiopathic cases in this study had no differences from findings in studies performed in various populations , as in this Canadian study Etiologic classification was symptomatic for 51 cases (68%), cryptogenic for 18 (24%), and idiopathic in six children (8%). (P.M. Brna, K.E. Gordon et al. 2001)<sup>12</sup> , the study of (Ibrahim shahnaz ,et al. 2010)<sup>13</sup> in Pakistan reveal 64.3% cases were identified as symptomatic while 19.6% were cryptogenic and 16.1% were idiopathic. Study of (Trevathan E et al. 1999)<sup>14</sup> in Atlanta reveal the half of the children with IS had cryptogenic IS . Study of (Virginia Wong 2001)<sup>11</sup> in Hong Kong she found idiopathic (N=19, 18%), cryptogenic (N=23; 22%), symptomatic (N=56; 53.3%) and unknown (N=7; 5.7%).

Outcomes in this study had same prognosis with studies in others populations, six patients in this study had been evolved to severe intractable seizures 18.75%; four patients had spastic quadriplegia 12.5%. Two patients had Hemiparesis 6.25%. 16 patients had severe developmental delay 50%. Four patients had mild to moderate mental retardation 12.5%. in study of (Kenton R et al. 1997)<sup>7</sup> carried out in south Carolina , USA , reveal developed later in 21 of 25 (84%) , various types of cerebral palsy

in 21 of 25 (84%), and mild, moderate, or severe mental retardation in 23 of 25 (92%). in study ( Glaze DG, Hrachovy RA, Frost JD Jr, Kellaway P, Zion TE 1988)<sup>15</sup> report that the overall prognosis for long-term outcome in these patients with infantile spasms was poor.

The adverse reactions of medications that were seen In this study are gastro-intestinal symptoms ( vomiting ) , and feeding problems , obesity, over-weight . These are common and not serious, study of (Rantala H. Putkonen T 1999)<sup>16</sup> report many adverse reactions because the large doses of ACTH and prednisolone used in therapeutic protocols, in this study we are use low doses steroids protocol.

### CONCLUSION:

1. Male to female ratio is 1:1.
2. Peak age of onset was 4-10 month.
3. Flexor type is commonest clinical types.
4. Symptomatic group is predominant etiological types.
5. Neurocutaneous syndrome is commonest cause in symptomatic group
6. Hypsarrhythmia is documented in majority of patients.
7. Brain atrophy is the commonest in radiological films.
8. Steroids are main treatment.
9. Infantile spasms had poor prognosis, in terms of neurobehavioral development.

### Recommendations:

- High index of suspicion of infantile spasms in those below one year with abnormal movement should be high , as the early detection and institute the treatment may improve the outcome .
- More time needed for proper follow up.
- Management the patients with infantile spasms should be optimized , depending on the major causes which is neurocutaneous disorders , no need for furthers investigations especially when skin examination denote clues to diagnosis .
- Investigations of suspected metabolic disorders should be done , because of availability of effective diet regimens for large list of inborn error of metabolism .
- Early treatment with steroids for idiopathic cases may have better outcome.

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