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Original Research Article.

A Study to Evaluate the Clinical Profile of Patients with West Syndrome

Latika Banshiwala[1], Jay Dhadke[2*], Shilpa Kulkarni[3]

[1]**Junior Resident, Department of Paediatrics,**
Seth G. S. Medical College and B. J. Wadia Hospital, Mumbai, Maharashtra, India.
[2]**Junior Resident, Department of Paediatrics,**
Dr. Vaishampayan Memorial Government Medical College, Solapur, Maharashtra, India.
[3]**Additional Professor, Department of Paediatrics,**
Seth G. S. Medical College and B. J. Wadia Hospital, Mumbai, Maharashtra, India.

ABSTRACT

Background: West Syndrome is an epilepsy syndrome comprising the triad of infantile spasms, an interictal electroencephalogram (EEG) pattern termed hypsarrhythmia and neurological regression. The aim of the present study to study the clinical profile of patients with West Syndrome.

Materials and Methods: The present study was conducted among 100 patients at B. J. Wadia Hospital for children, a tertiary care teaching hospital at Parel, Mumbai over a period of 18-24 months. Complete history was taken. Based on etiology West syndrome was classified as symptomatic (known etiology) or cryptogenic (unknown etiology). Following tests will be used to find correlation between different parameters with the above outcome – one-way ANNOVA, unpaired t- test, Mean Whitney test, chi-square test and Kruskal Wallis.

Results: In the present study total number of patients studied included in the study were 100.The mean age at which patients with infantile spasms presented to our hospital was 8.9 months while the age of onset of spasms were 6 months. Male: Female ratio was 3.5:1. Etiology of West syndrome was identified in 74% children (Symptomatic) and 26% remained cryptogenic and idiopathic. The etiology of infantile spasms commonest being birth asphyxia (HIE) ;4 patients had history of meningitis in neonatal period; 2 were diagnosed with tuberous sclerosis and 4 with some brain deformity based on neuroimaging; and 1 with TORCH infection. Frequency distribution of behaviour abnormalities and other evolving seizure types (over the follow-up years) among the patients was less.

Conclusion: Our study concluded that Symptomatic West Syndrome was the most common type, hypoxic ischaemic encephalopathy being the commonest etiology of it.

Keywords: West Syndrome, Epilepsy Syndrome, Microcephaly.

***Correspondence to:**

Dr. Jay Dhadke,
Junior Resident,
Department of Paediatrics,
Dr. Vaishampayan Memorial Government Medical College,
Solapur, Maharashtra, India.

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INTRODUCTION

West Syndrome is an infantile epilepsy syndrome composed of the triad of infantile spasms, an interictal electroencephalogram (EEG) pattern termed hypsarrhythmia and neurological regression.[1] The clinical aspect was first explained by English Paediatrician W J West in 1841 who witnessed the condition for the first time in his own child. He described the movements as "brief, flexor and axial, mainly involving the neck, and they occurred in clusters. He described the mental deterioration and emphasized intractability, noting that all his therapeutic trials had been of no benefit."[2,3]

The incidence of WS is well documented in developed countries, and a study in Finland reported an estimated incidence of 30.7 per 100,000 live births.[1] There has been an increased understanding of the role of genetic defects in the etiology of infantile spasms, such that there are panels of genetic mutations that are commercially available for testing. In addition to the genetic mutations in TSC1 and TSC2, which cause tuberous sclerosis, specific genetic defects have been identified in many patients with early onset of infantile spasms, including mutations in the gene ARX on the short arm of chromosome X[4], which is associated with a wide variety of structural brain abnormalities, and a mutation in the cyclin-dependent kinase-like protein 5 (CDKL5).[5,6] Neuro-radiological investigations has a key role in search of etiology in determining a precise etiology, to know the prognosis and to orient the therapeutic approach, since some patients need specific drug treatments, whereas others may be candidates for surgery.

Delayed myelination seems to be independent of specific etiology and can be present at the onset of cryptogenic West syndrome.[7] The aim of the present study to study the clinical profile of patients with West Syndrome.

MATERIALS AND METHODS

The present study was conducted among 100 patients at B. J. Wadia Hospital for children, a tertiary care teaching hospital at Parel, Mumbai over a period of 18-24 months. It includes patients diagnosed with west syndrome, based on clinical presentation of infantile spasms and electroencephalographic (EEG) findings of hypsarrhythmia or modified hypsarrhythmia and developmental regression.

Patients whose medical records of follow up are of less than 6 months and patients whose parents did not consent for participation were excluded from the study. Hypsarrhythmia was defined as EEG showing high-voltage chaotic slow waves intermixed with spike and sharp wave discharges. Modified Hypsarrhythmia was defined in presence of any of the following: increased interhemispheric synchronization-consistent voltage asymmetries; consistent focus of abnormal discharge; episodes of generalized/regional or lateralized voltage attenuation; or primarily high voltage bilaterally asynchronous slow wave activity.

From each patient file following data will be retrieved-

- Sex of patient
- Reported age at the onset of infantile spasms
- Age at diagnosis and start of treatment of west syndrome
- Type of seizures before diagnosis of west syndrome
- Ages at subsequent follow up visits
- Developmental quotient at the time of diagnosis of WS and at last visit
- Birth history including relevant antenatal and perinatal history
- History of sleep problems, feeding problems, visual or hearing impairment, behavioral problems and repeated chest infections was also noted
- Physical examination findings suggestive of cerebral palsy, microcephaly, presence of neurocutaneous markers, dysmorphism and organomegaly.

Development Quotient was recorded at the time of diagnosis of West syndrome and at follow up visits. Development Quotient is the numerical expression of a child's development level as measured by dividing the developmental age by the chronological age and multiplying by 100. Seizure frequency was recorded at each follow up visit in terms of average number of spasms per cluster and number of clusters per day; to see for efficacy of treatment. Two categories accordingly-favourable and unfavourable were made. The outcome was considered favorable when there was a more than 80% spasm control in less than 6 months without relapse or progression to other seizure types. EEG was repeated in patients who relapsed or progressed to have other seizure types and in those with spasm cessation to document resolution of hypsarrhythmia. The presence of favorable outcome was studied in relation to etiology and clinical variables at presentation. The results of EEG and neuro imaging were noted. Neuro-imaging (CT Scan and MRI) was the initial investigation in children where there was a clear history suggestive of perinatal insults, postnatal meningitis or encephalitis. Based on etiology West syndrome was classified as symptomatic (known etiology) or cryptogenic (unknown etiology). Following tests will be used to find correlation between different parameters with the above outcome – one-way ANNOVA, unpaired t- test, Mean Whitney test, chi-square test and Kruskal Wallis.

RESULTS

In the present study total number of patients studied included in the study were 100 in which 78% were males and 22% were females. Total number of patients studied included in the study were 100. The mean age at which patients with infantile spasms presented to our hospital was 8.9 months (range 5months to 24 months)while the age of onset of spasms were 6 months (range-0 months to 15 months) Male: Female ratio was 3.5:1.Etiology of West syndrome was identified in 74% children (Symptomatic) and 26% remained cryptogenic and idiopathic. The etiology of infantile spasms commonest being birth asphyxia (HIE) [54%]; 4 patients had history of meningitis in neonatal period; 2 were diagnosed with tuberous sclerosis and 4 with some brain deformity based on neuroimaging; and 1 with TORCH infection.

Table 1. Association Between Outcome of Child and Gender

Gender		Outcome of child		Total
		Favourable	Unfavourable	
Male	**n**	37	41	78
	%	47.4%	52.6%	100.0%
Female	**n**	6	16	22
	%	27.3%	72.7%	100.0%
Total	**n**	43	57	100
	%	43.0%	57.0%	100.0%

	Value	df	p value
Pearson Chi-Square	2.846a	1	.092

Table 2. Association Between Outcome of Child and Type of West syndrome

Type of West syndrome		Outcome of child		Total
		Favourable	Unfavourable	
Cryptogenic West Syndrome	N	13	9	22
	%	59.1%	40.9%	100.0%
Symptomatic West Syndrome	N	26	48	74
	%	35.1%	64.9%	100.0%
Idiopathic West Syndrome	N	4	0	4
	%	100.0%	0.0%	100.0%
Total	N	43	57	100
	%	43.0%	57.0%	100.0%

	Value	df	p value
Pearson Chi-Square	9.494a	2	.009
Yates Continuity Correction			.004

Table 3. Distribution of etiology if Symptomatic WS among all patient

Etiology if symptomatic WS	Frequency	Percentage
Haemorrhage	2	2.8%
Brain deformity	4	5.6%
Hypoglycemic seizure	4	5.6%
Hypoxic ischaemic encephalopathy	54	76.0%
Meningitis	4	5.6%
TORCH	1	1.4%
Tuberous Sclerosis	2	2.8%
Total	71	100.0%

Table 4. Association Between Outcome of Child and Type of spasms

Type of spasms		Outcome of child		Total
		Favourable	Unfavourable	
Flexor Spasm	n	30	31	61
	%	49.2%	50.8%	100.0%
Extensor Spasm	n	5	8	13
	%	38.5%	61.5%	100.0%
Mixed Spasm	n	8	18	26
	%	30.8%	69.2%	100.0%
Total	n	43	57	100
	%	43.0%	57.0%	100.0%

	Value	df	p value
Pearson Chi-Square	2.647a	2	.266

Table 5. Association Between Outcome of Child and Consanguinity

Consanguinity		Outcome of child		Total
		Favourable	Unfavourable	
Present	n	4	6	10
	%	40.0%	60.0%	100.0%
Absent	n	39	51	90
	%	43.3%	56.7%	100.0%
Total	n	43	57	100
	%	43.0%	57.0%	100.0%

	Value	df	p value
Pearson Chi-Square	.041	1	.840
Fisher's Exact Test			.999

Table 6. Distribution of Significant ANC history among all patients

Significant ANC history	Frequency	Percentage
Yes	4	4.0%
No	96	96.0%
Total	100	100.0%

Table 7. Association Between Outcome of Child and Mode of delivery

Mode of delivery		Outcome of child		Total
		Favourable	Unfavourable	
LSCS	**n**	6	16	22
	%	27.3%	72.7%	100.0%
Vaginal	**n**	37	41	78
	%	47.4%	52.6%	100.0%
Total	**n**	43	57	100
	%	43.0%	57.0%	100.0%

	Value	df	p value
Pearson Chi-Square	2.846	1	.092
Fisher's Exact Test			.143

Table 8. Association Between Outcome of Child and Term

Pre-term/Term		Outcome of child		Total
		Favourable	Unfavourable	
Pre Term	**n**	2	3	5
	%	40.0%	60.0%	100.0%
Term	**n**	41	54	95
	%	43.2%	56.8%	100.0%
Total	**n**	43	57	100
	%	43.0%	57.0%	100.0%

	Value	df	p value
Pearson Chi-Square	.019	1	.889
Fisher's Exact Test			.889

Table 9. Association Between Outcome of Child and History of birth asphyxia

History of birth asphyxia		Outcome of child		Total
		Favourable	Unfavourable	
Yes	**n**	16	39	55
	%	29.1%	70.9%	100.0%
No	**n**	27	18	45
	%	60.0%	40.0%	100.0%
Total	**n**	43	57	100
	%	43.0%	57.0%	100.0%

	Value	df	p value
Pearson Chi-Square	9.647	1	.002

Table 10. Association Between Outcome of Child and Microcephaly

Microcephaly		Outcome of child		Total
		Favourable	Unfavourable	
Yes	n	6	23	29
	%	14.3%	67.6%	38.2%
No	n	36	11	47
	%	85.7%	32.4%	61.8%
Total	n	42	34	76
	%	100.0%	100.0%	100.0%

	Value	df	p value
Pearson Chi-Square	22.673a	1	<0.001
Fisher's Exact Test	20.467		**<0.001**

Table 11. Association Between Outcome of Child and Results of BERA

BERA		Outcome of child		Total
		Favourable	Unfavourable	
Normal	N	11	11	22
	%	50.0%	50.0%	100.0%
Hearing loss	N	0	4	4
	%	100.0%	100.0%	100.0%
Not Done	N	32	42	74
	%	43.2%	56.8%	100.0%
Total	N	43	57	100
	%	43.0%	57.0%	100.0%

	Value	df	p value
Pearson Chi-Square	3.49	2	.177
Pearson Chi-Square (Excluding Not Done Gp)	3.467	1	.060
Fishers Exact test (Excluding Not Done Gp)			.182

Table 12. Association Between Outcome of Child and Behavioural issues

Behavioural issues		Outcome of child		Total
		Favourable	Unfavourable	
Yes	n	8	6	14
	%	57.1%	42.9%	100.0%
No	n	35	51	86
	%	40.7%	59.3%	100.0%
Total	n	43	57	100
	%	43.0%	57.0%	100.0%

	Value	df	p value
Pearson Chi-Square	1.328a	1	.249
Fisher's Exact Test			.263

Table 13. Association Between Outcome of Child and Other evolving seizure type

Other evolving seizure type		Outcome of child		Total
		Favourable	Unfavourable	
Yes	n	1	14	15
	%	6.7%	93.3%	100.0%
No	n	42	43	85
	%	49.4%	50.6%	100.0%
Total	n	43	57	100
	%	43.0%	57.0%	100.0%

	Value	df	p value
Pearson Chi-Square	9.505a	1	.002
Fisher's Exact Test			.002

Table 14. Association Between Outcome of Child and Development quotient at follow-up visits

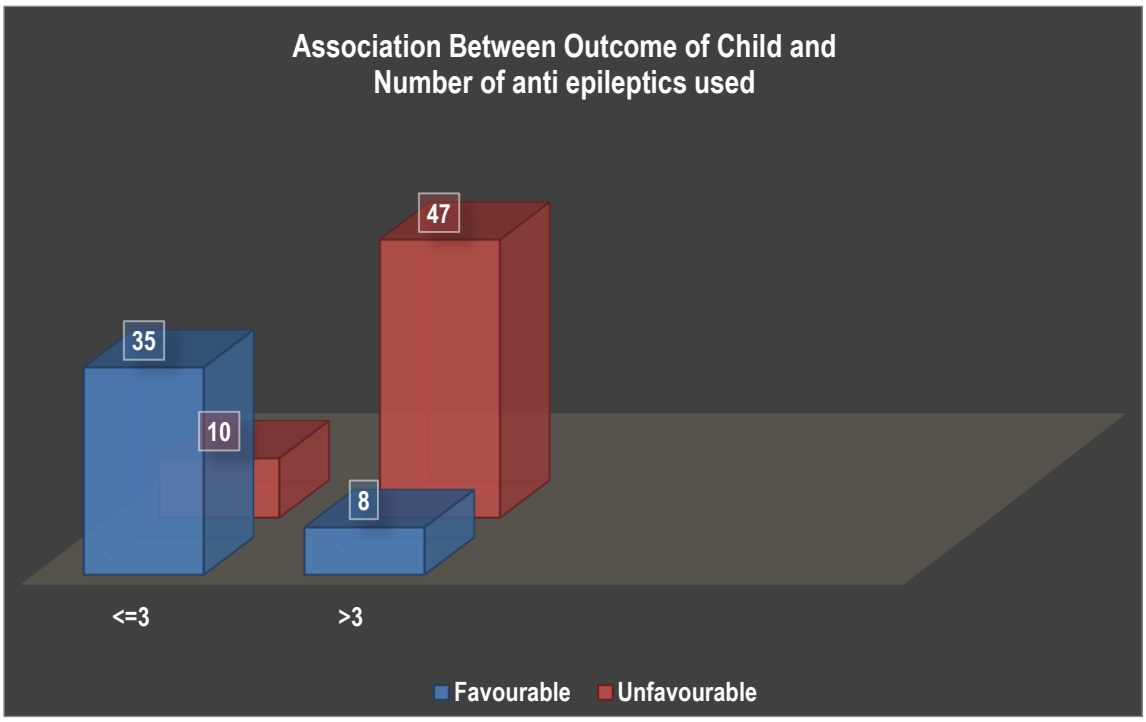
Development quotient at follow-up visits		Outcome of child		Total
		Favourable	Unfavourable	
Improved	n	42	14	56
	%	75.0%	25.0%	100.0%
Not Improved	n	1	43	44
	%	2.3%	97.7%	100.0%
Total	n	43	57	100
	%	43.0%	57.0%	100.0%

	Value	df	p value
Pearson Chi-Square	53.173a	1	.000
Fisher's Exact Test			.000

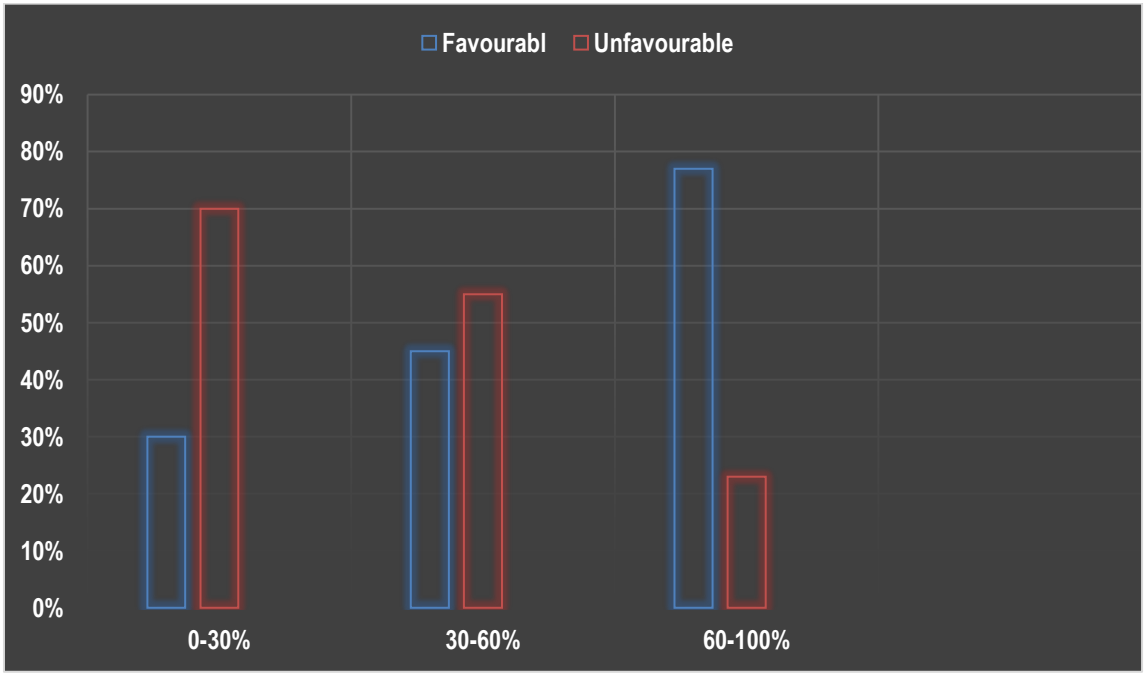
Table 15. Association Between Outcome of Child and Ophthalmic Evaluation

Ophthalmic evaluation		Outcome of child		Total
		Favourable	Unfavourable	
Normal	N	11	8	19
	%	57.9%	42.1%	100.0%
Abnormal	N	4	13	17
	%	23.5%	76.5%	100.0%
Not Done	N	28	36	64
	%	43.8%	56.3%	100.0%
Total	N	43	57	100
	%	43.0%	57.0%	100.0%

	Value	df	p value
Pearson Chi-Square	4.364	2	.112
Pearson Chi-Square (Excluding Not Done Gp)	4.35	1	.030
Fishers Exact test (Excluding Not Done Gp)	4.23	1	.040



Graph 1: Association between outcome of child and number of anti-epileptics used



Graph 2: Association between outcome and DQ at onset

Table 16. Association Between Outcome of Child and Improvement of EEG at f/u visit

EEG at f/u visit		Outcome of child		Total
		Favourable	Unfavourable	
Improved	n	18	6	24
	%	81.8%	25.0%	52.2%
Not Improved	n	4	18	22
	%	18.2%	75.0%	47.8%
Total	n	22	24	46
	%	100.0%	100.0%	100.0%

	Value	df	p value
Pearson Chi-Square	14.850a	1	<0.001
Fisher's Exact Test			**<0.001**

Table 17. Mean and Median comparison of age at onset, lag of onset and diagnosis and total follow up period and other quantitative variables between Improvement in DQ at follow Up

Development quotient at follow-up visits	Improved (n=56)			Not Improved (n=44)			Mann Whitney U	Z	p valve
	Mean	Median	SD	Mean	Median	SD			
Age on presentation (in months)	11.03	8.75	7.35	11.56	9.00	6.53	1158.0	-0.52	0.606
Age at onset of spasms (in months)	6.05	5.00	3.21	5.61	3.50	4.41	899.0	-2.32	**0.020**
Age at diagnosis of spasms (in months)	8.69	6.75	5.30	9.57	8.00	6.14	1124.0	-0.75	0.451
Lag of onset and diagnosis (in months)	2.78	1.00	5.10	3.72	3.00	3.79	956.5	-1.97	**0.049**
Age at start of treatment (in months)	9.20	7.00	5.47	10.13	8.00	6.26	1123.5	-0.76	0.449
Lag of diagnosis and treatment (in months)	0.65	0.00	1.51	0.88	0.00	2.05	1130.0	-0.88	0.376
No of antiepileptics Used	1.00	1.00	0.00	2.00	2.00	0.00	513.5	-5.07	**<0.001**
Development Quotient at first visit	47.2%	50.0%	31.1%	27.5%	30.0%	25.0%	768.0	-3.24	**0.001**
Total follow up period (in months)	24.75	24.00	10.11	28.09	24.00	8.75	879.0	-2.57	**0.010**

Table 18: Comparison between mean and median of lag of onset and diagnosis between different seizure frequency groups

Seizure Frequency at Follow Up	> 80%			50-80%			<50%			Chi Square (Kruskal Walis H test)	p value
	Mean	Median	SD	Mean	Median	SD	Mean	Median	SD		
Lag of onset and diagnosis (in months)	1.06	0.50	1.68	2.79	1.00	3.29	5.65	5.00	5.85	17.0	**<0.001**

DISCUSSION

West Syndrome is a major type of infantile epilepsy but there is a paucity of data regarding the prognostic consequences of this syndrome. This is a retrospective study of 100 children with West syndrome conducted at a tertiary level hospital of Western India. This study highlights the clinical spectrum and the predictors of outcome in children with West Syndrome, hence providing a developing country's perspective.

The mean age at onset of infantile spasms in our study is 6.0 months, which is comparable to experience in other centres.[8-10] The mean lag time in diagnosis and onset of these spasms found in our study is 1.06 months. It is higher in developing country like ours, likely owing to the delayed health-seeking behaviour of parents and administration of inappropriate anti-epileptics such as phenobarbitone, phenytoin and carbamazepine. These have previously been acknowledged as lacunae in the treatment and the resultant poor outcome in children with West Syndrome in developing counties.[11,12] We found significant association in our study between the lag of onset and diagnosis with the unfavourable seizure outcome with p value of <0.001 and poor developmental outcome with p value of 0.049.

Striking male preponderance was found in our study (78% of patients), probably owing to gender-biased referral and treatment-seeking behaviour of parents in our country. These findings are similar to other studies in Indian sub-continent.[12,13] But in our study, gender does not seem to affect the neuro-outcome of the disease.

Significant association was seen between microcephaly at the time of presentation and the unfavourable outcome with the p value of .001.[11-13]

Etiology of West Syndrome was identified in 74% children (Symptomatic) and 26% remained cryptogenic and idiopathic in our study. The etiological profile was considerably different in our study as compared from the western studies. The most common cause was a perinatal brain injury, especially perinatal asphyxia (in 54 patients) and also it was found that history of birth asphyxia was present in more than half of the patients (55%) depicting a probable correctable etiology of West syndrome. This has been the conclusion in some of the previous studies of Matsuo et al.,[14] Kalra& Passi,[15] Mackay et al.,[16] Tsuji et al.,[17] Kaushik et al.).[18] In contrast, prenatal causes which includes neurocutaneous markers like tuberous sclerosis, cortical malformations and genetic-metabolic disorders are the predominant etiologies in the West.[18] In our study setting, high incidence of perinatal asphyxia could be attributed to high rates of home delivery, delivery by unskilled workers, lack of adequate antenatal care, delay in treatment initiation and poor referral system. Improvement in the maternal and neonatal health services may help in reducing the incidence of West syndrome in developing country.

15% of our patients developed other seizure types including generalized tonic seizures, focal seizures and minor motor type seizures during our follow-up period. There were behavioural issues like ADHD, autistic behaviour etc which was noticed by the parents during the follow-up period in 14% of the patients.

High rate of co-morbidities such as vision and hearing impairment, as sequelae of peri-natal insult are additional problems in children with West syndrome but the conclusive data is not found due to incomplete records available.

The limitations of the study include the lack of long term follow up of the patients.

CONCLUSION

Our study concluded that Symptomatic West Syndrome was the most common type, hypoxic ischaemic encephalopathy being the commonest etiology of it.

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