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Original Research Article

Correlation of neuroimaging findings and outcome in West syndrome

Bina Prajapati Manandhar, Divya K. C.*, Najala Khatun

Department of Pediatrics, International Friendship Children's Hospital, Kathmandu, Nepal

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***Correspondence:**
Dr. Divya K. C.,
E-mail: 44divyakc@gmail.com

ABSTRACT

Background: West syndrome (WS), an infantile epileptic encephalopathy which occurs in clusters with developmental regression and hypsarrhythmia. The classification refers to genetic, structural and metabolic cause. Neuroimaging can help to identify various lesion in the brain leading to West syndrome and outcomes can be measured in form of seizure control and neurodevelopmental improvement. We aimed to study the correlation of neuroimaging in West syndrome with the outcomes.
Methods: This was a retrospective cross-sectional study done among patients who presented to International friendship children's hospital. All the cases diagnosed with WS and between 4 months to 5 years of age according to ILAE (International league against epilepsy) were included in this study. The study duration was three years. Fisher's exact test was used to see correlation of underlying neuroimaging findings with outcome in children with West syndrome.
Results: Of 37 children diagnosed with WS, 65% were male with a mean age of presentation 17±7 months and mean age of onset of seizure 5±1 months. Thirty patients had regular follow up and neurodevelopmental outcome could be determined. There was no significant relation between neuroimaging finding and neurodevelopmental outcome along with seizure remission ($p>0.05$). Improvement in developmental milestones was seen in 17 patients (56.6%) and 1 patient (3.3%) had normal milestone as per age.
Conclusions: Neuroimaging is an important diagnostic tool to determine etiology of WS but it's not the sole component to predict the neurodevelopmental outcome and seizure remission.

Keywords: West syndrome, Neuroimaging, Neurodevelopment

INTRODUCTION

WS is the most frequently occurring infantile epileptic encephalopathy. Most cases typically present with triad of infantile epileptic spasms that usually occur in clusters (particularly in drowsiness or upon arousal), developmental regression and a typical EEG picture called hypsarrhythmia.[1] Spasms can be described as an abrupt often clustered, extension, flexion or mixed extension flexion movement primarily involving the proximal and truncal muscles.[2] The age of onset is usually between 2-12 months.[1] It can occur in children of all ethnic groups.

The term WS was 1st coined by the English physician, William James West in 1841 in the scientific journal The Lancet, of his clinical experience with the condition on his own son James Edwin West, aged 4 months at the time of onset of his first seizures.[3]

The exact pathophysiology of infantile spasm is unknown. One of the postulated hypotheses suggested that infantile spasms resulted from a nonspecific insult at a critical point in the ontogenetic development of the brain.[4] The worldwide incidence is 1.6 to 4.5 per 10,000 live births.[5-8] The incidence of WS in Asia is 0.18 per 1000 live births.[9]

Traditionally, infantile spasms have been classified as idiopathic, symptomatic and cryptogenic but currently the classification refers to genetic, structural and metabolic cause.[10] Conditions that have been identified as etiologic or predisposing factors for WS include trauma, infections, neoplasms, genetic aberrations, toxins and hypoxia/ischemia.[4] The symptomatic or structural/metabolic group of WS has patients with numerous types of brain anomalies which has varied prognosis along with evolutional changes as per different type of anomalies.[11]

The prognosis of infantile spasm is multifactorial and depends on the underlying cause, that is, congenital brain malformation; electroencephalography pattern; the appearance of seizures prior to the spasms; and a rapid response to treatment.[12] Cryptogenic/unknown and idiopathic/genetic causes of West syndrome have more favorable outcomes.[13,14]

Most patients with WS suffer a poor prognosis leading to mental retardation, chronic epilepsy and other neurodevelopmental disabilities.[3]

CT scan and MRI have made major contributions to the understanding of structural lesion causing WS. Seizure prognosis and outcome depends on the type of brain lesion thus early neuroimaging can help to choose appropriate antiepileptic.

Treatment options for WS include antiepileptics such as sodium valproate, topiramate, levetiracetam along with ACTH, prednisolone and vigabatrin.[11]

Many of the South Asian countries like Nepal lack published literature regarding WS. It is prudent to know the underlying cause and mechanism of WS for treatment and explanation of the prognosis. Neuroimaging can help us to identify various lesion in the brain leading to west syndrome and thus we can specify the outcomes in form of seizure control and neurodevelopmental improvement. Therefore, the objective of this study was to know the correlation of neuroimaging in WS with the outcomes.

METHODS

This retrospective cross-sectional study was carried out in the inpatient and outpatient in International friendship children's hospital, Kathmandu, Nepal for a period of 3 years and 1 month (March 2018 to April 2021). Ethical approval was taken prior to data collection.

All patients who were diagnosed as a case of WS in between age of 4 months to 5 years according to ILAE were included in this study. A total of 42 patients who matched the inclusion criteria were included among which 5 were removed from the study due to unavailability of neuroimaging findings. All patients without consent and incomplete workup were excluded. The participants required follow up for at least 6 months.

The patients were properly evaluated by taking a thorough history of seizures, associated neuro-developmental problems, pregnancy and birth related problems, neonatal problems, history of early development and family were collected from the patients' parents. Neurodevelopmental assessment was done by clinical judgment at time of diagnosis and on follow up, progress was noted. The electroencephalographic and neuroimaging either CT scan or MRI of brain findings were also collected. Their treatment history and status on follow up was noted. Seizure remission rate was calculated and expressed in percentage from the baseline number of episodes of seizure in 24 hours.

The data were collected and entered into Microsoft excel sheet for preliminary checking and editing.

Statistical Package for Social Sciences (SPSS), version 25 was used for data analysis. Fischer-exact test was used to see correlation of neuroimaging with neurodevelopmental outcomes and seizure remission in children with WS, value of ≤0.05 was considered as statistically significant.

RESULTS

A total of 37 cases of diagnosed WS were included in this study. Most of them were male 24 (64.9%). Maximum patients were between 0-12 months with mean age of 17±7 months. The minimum age of presentation was 2 months whereas maximum was 55 months (Figure 1). The mean age of onset of seizure was 5±1 month.

Table 1: Etiologic classification.

Eitology	N (%)
Cryptogenic	6 (16.2)
Perinatal asphyxia	10 (27.0)
Neonatal sepsis/neonatal meningitis	6 (16.2)
Hypoglycemia	5 (13.5)
Congenital brain malformation	4 (10.8)
Kernicterus	5 (13.5)
Downs phenotype	1 (2.7)

Table 2: EEG abnormalities of studied population.

EEG abnormalities	N (%)
Hysparrythmia	27 (73)
Epileptic encephalopathy	7 (18.9)
Focal discharge	3 (8.1)

History of perinatal asphyxia was evident among 10 (27%) of the total cases. Among the total patients 4 (10.8%) were preterm and 24 cases (64.9%) term.

Among the total 37 children presenting with WS, typical EEG of hysparrthymia was seen in 27 (73%) patients (Table 2).

A total of 24 cases had history of NICU stay due to various causes and 8 cases (21.6%) had postnatal problems for which NICU stay was not done. The most common cause of NICU admission was birth asphyxia with NNS a total of 5 cases (Figure 2).

MRI head was done in 25 (67.6%) patients, CT scan head was done in 11 (29.7%) patients and both was done in 1 (2.7%) patient.

Neuroimaging finding which was commonly found was encephalomalacia with gliosis (Table 3).

Behavioral problems such as autism was seen in 5 (13.5%) of the patients.

Various ophthalmologic problems were seen among total 37 patients of which the most common was cortical blindness in 7 (24.3%) of total (Figure 3).

Developmental delay which was a component of WS was seen in most all of the patients that was a total of 23 (62%) patients with GDD and 9 (24%) with GDD and visual defect.

While comparing the neuroimaging findings with the neurodevelopmental it was found that there was no statistical significance. Any underlying abnormality had no relation with global developmental delay.

Table 3: Neuroimaging abnormalities of studied population.

Abnormal neuroimaging findings	N (%)
Congenital malformation	4 (10.8)
Porencephalic cyst	2
Schizencephaly with porencephalic cyst	1
Pachygyria	1
Hypoxic injury	19 (51.3)
Encephalomalacia with gliosis	8
Encephalomalacia	3
Heterogenous hyperintense signal	3
Gliosis	2
Diffuse atrophy	1
Periventricular leukomalacia	1
Encephalomalaicia with atrophy	1
Calcification	4 (10.8)
Tuberous sclerosis	2
Periventricular calcific foci	1
Parietal lobe calcific foci	1
Normal	10 (27)
Total	37

Table 4: Correlation between neuroimaging finding and neurodevelopmental outcome at time of diagnosis.

Neuroimaging findings	GDD	Visual defect	Speech delay	GDD and visual defect	Motor delay
Congenital malformation	4	0	0	0	0
Hypoxic injury	9	3	0	7	0
Calcification	3	0	0	1	0
Normal	7	0	1	1	1
Total	23	3	1	9	1

Table 5: Correlation between neuroimaging finding and neurodevelopmental outcome at 6 months follow up.

Neuroimaging findings	GDD	Visual defect	Speech delay	GDD and visual defect	Normal
Congenital malformation	3	0	0	0	0
Hypoxic injury	10	2	0	3	0
Calcification	2	0	0	1	0
Normal	7	0	1	0	1
Total	22	2	1	4	1

Table 6: Correlation of neuroimaging and neurodevelopmental progression.

Correlation	Gaining milestones	No improvement	Milestones as per age
Congenital malformation	1	2	0
Hypoxic injury	9	6	0
Calcification	1	2	0
Normal	6	2	1
Total	17	12	1

Table 7: Correlation between neuroimaging finding and seizure remission at 6 months follow up.

Neuroimaging findings	0%	<25%	25-<50%	50-<75%	100%
Congenital malformation	0	0	0	1	2
Hypoxic injury	0	3	2	2	8
Calcification	0	0	0	2	1
Normal	1	0	1	1	6
Total	1	3	3	6	17

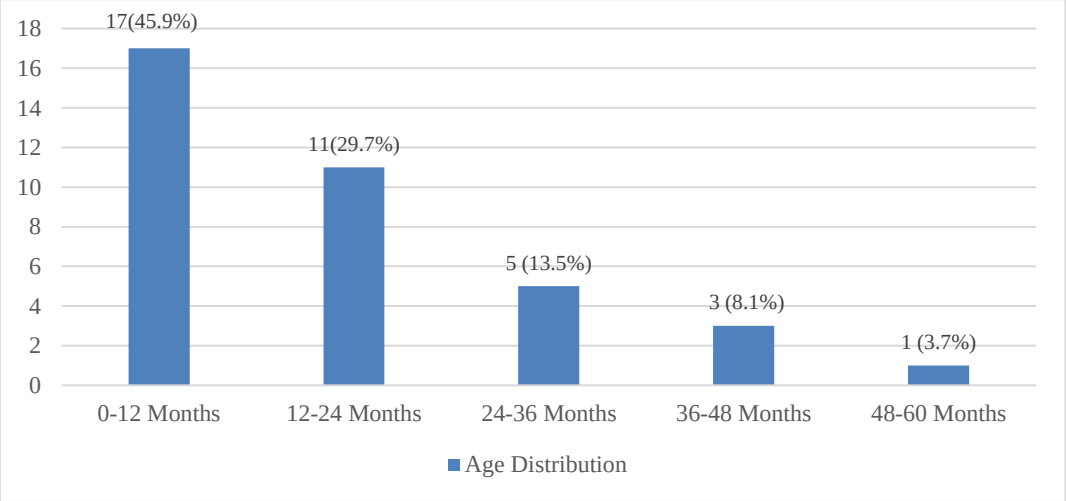

Figure 1: Age of presentation.

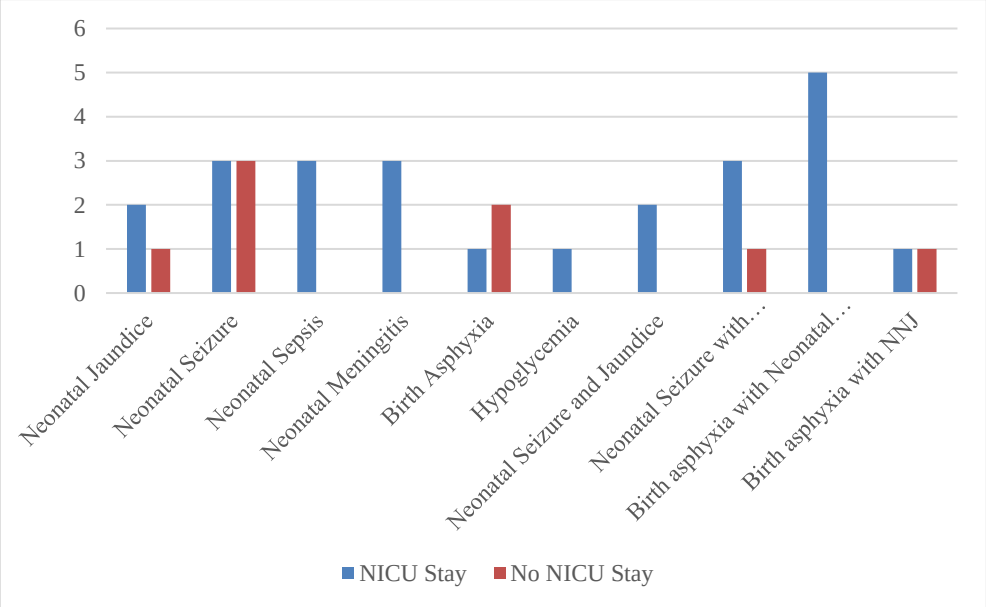

Figure 2: Postnatal problems and NICU stay.

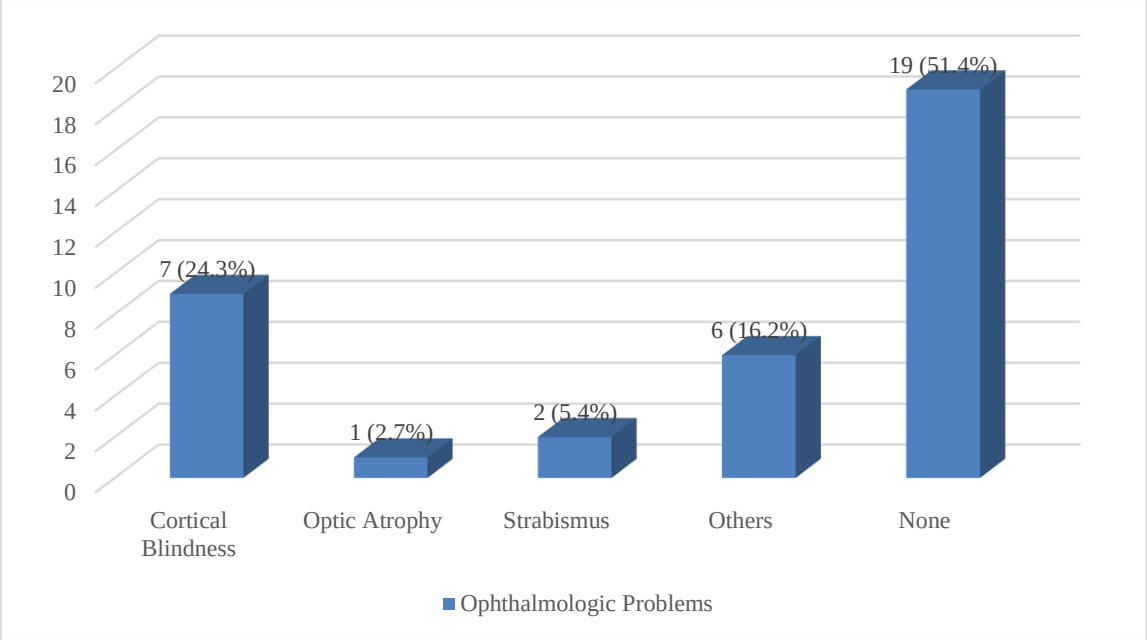

Figure 3: Ophthalmologic problems in studied population.

Neurodevelopment outcome at 6 months of treatment and seizure reduction could only be done for 30 patients as there were 2 mortalities within 2 months of diagnosis and 5 patients did not have regular follow up (Table 4).

While comparing the neuroimaging findings with the neurodevelopmental outcome it was found that there was no statistical significant correlation (p>0.05). Any underlying abnormality had no relation with global developmental delay. 22 (73.3%) cases had global developmental delay whereas 4 (13.33%) had GDD with visual defects (Table 5).

Around 17 (56.6%) of total patients had improvement in developmental milestones whereas 1 (3.3%) had normal milestone as per age. It was seen that most cases which had normal radiologic findings were gaining milestones and those with congenital malformation and calcifications had less improvement (Table 6).

There was no significant relation between reduction in episodes of seizure and type of lesion. P value was >0.05. Seizure remission was seen in most cases with normal neuroradiologic finding (Table 7).

Steroid was the most common drug used to treat WS and reduction in episodes of seizure was seen in patient where steroids alone or in combination of antiepileptics (commonly sodium valproate) were used but this was not statistically significant (p>0.05). In two cases of tuberous sclerosis, vigabatrin was used which resulted in complete resolution of seizures but one case was lost in follow up thus was not included.

DISCUSSION

The retrospective analysis of patients for this study had shown that male predominance was present which was also seen in other studies like Akter et al.[11] Mean age of seizure onset was 5±1 month which can be comparable to findings of study done by Lagae et al.[15]

Among the given causes of WS, perinatal asphyxia was present in 10 (27%) of the total patients which was lesser than that of other study done by Barbarrosa et al.[16] Other causes were postnatal infections, meningitis, kernicterus, tuberous sclerosis and congenital brain anomalies which was also seen in study done by Barbarrosa et al and Sharma et al.[15,17] Tandem mass spectrometry was done in 3 cases where cause could not be determined but results were normal. In the remaining cases this test could not be done due to patients' financial instability thus, neurometabolic causes for WS couldn't be ruled out.

EEG was done in all the studied population where a typical EEG pattern of hysparrthymia was seen in 73% patients followed by epileptic encephalopathy seen in 18.9%. Other EEG patterns such as asymmetric features, focal discharges and semi-periodic burst-suppression were also seen in WS which was defined as atypical or modified hypsarrhythmia.[18]

Neuroimaging findings were seen in 73% of the cases which was similar to that of a study done by Khatami et al.[8] The most common cause was hypoxic injury with a total of 16 (43.3%) cases among which 10 had history of delayed cry. Calcifications were detected in 4 (10.8%) cases among which 2 were diagnosed as tuberous

sclerosis. There was one diagnosed case of Down's syndrome which had normal neuroimaging findings. There were 3 cases of hyperintense signal with demyelination but underlying cause could not be determined and hypoxia was presumed cause for these cases. Congenital malformation that detected were 1 case of schizencephaly, 2 cases of porencephalic cyst and 1 case of pachygyria.

It had been found that in west syndrome there was a risk of developing autism spectrum disorders.[12] In this study 5 (13.5%) of cases had autism.

Visual defects were present in most patients with WS, especially if the EEG was hypsarrhythmic.[19] Cortical visual impairment which was found commonly was seen in 7 (24.3%) cases in this study. Other visual problems found were strabismus, optic atrophy, disc pallor, absence of visual fixing.

In this study neurodevelopmental outcome at 6 months of follow up showed that around 86% had GDD (including those with visual defects) which was similar to the study done by Akter et al.[11] Neurodevelopment assessment could not be done by Standard development assessment tools due to unavailability of such instruments. In other study done by Gupta et al where developmental tools were used for assessment it was seen that 91% had moderate to severe developmental delay. Even though developmental tools were unavailable, clinical assessments were made to check development outcomes and it was observed that out of 30 patients seen in follow up 17 (56.6%) were improving, gaining milestones and 1 patient had normal milestones as per age. This improvement could have resulted from early diagnosis and treatment along with supportive medical as well as physiotherapy. There was no statistical significance regarding neurodevelopmental outcome and the type of neurologic lesion observed in this study.

The drugs that were commonly used for treatment were steroid and sodium valproate which showed a good response for seizure remission in the affected patients. Vigabatrin was used in two patients suffering from tuberous Sclerosis which was imported from other countries as the drug was not available in Nepal, a good response with seizure remission was observed in one patient and the other patient was lost on follow up. ACTH could not be used for treatment due to unavailability of the drug and cost issues as most patients couldn't afford it. Other drugs used were levetiracetam, phenobarbitone, topiramate and clonazepam. Pyridoxine was used for refractory seizures. No statistical significance could be observed with neuroradiologic abnormality and seizure remission as most cases could not get treatment at onset of disease due to the delay in presentation to the hospital and management.

It had been mentioned in various studies that a short lag in treatment of WS had favorable outcomes.[21,22] In our study we can see that the mean age of onset of seizure was 5 months whereas mean age of presentation was 17 months thus a favorable outcome could not be achieved due to delayed management.

There were 2 mortalities one was case of schizencephaly and one of hypoxic injury indicating poor prognosis in patients with any underlying cause congenital anomaly or any hypoxic insult.

Prognosis in WS was multifactorial but with help of neuroimaging and early diagnosis, cases which have treatable cause can be identified early and a proper plan for management can be formulated along with this proper counseling can be done to parents regarding child's disease condition.

Limitations

The limitations were that it was a retrospective study with small sample size. Few cases were lost on follow up which could have affected the results. Full diagnostic work up along with proper drug use could not be done due to economic condition of the patients' parents.

CONCLUSION

Neuroimaging is an important diagnostic tool to find out the causes of WS but it's not a sole measure to determine the neurodevelopmental outcome and resolution of spams. Seizure remission can be achieved if treatment is started immediately after onset of symptoms according to the underlying etiology of WS. The prognosis of WS depends on the cause, cryptogenic cause has better outcome than other causes, regular supervision and help is required for most children suffering from WS throughout life.

Recommendations

For every diagnosed case of WS early neuroimaging and treatment initiation is required. Similarly, a proper neurodevelopment assessment should be done to determine the future prognosis as well as to counsel the patients.

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