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Research Article

Clinical profile of neonatal seizures with special reference to biochemical abnormalities

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ABSTRACT

Background: Neonatal seizures are clinically significant because very few are idiopathic. Biochemical disturbances occur frequently in neonatal seizures either as an underlying cause or as associated abnormalities. Early recognition and treatment of these biochemical disturbances are essential for optimal management and satisfactory long term outcome. The main of the study is to assess the importance of biochemical abnormalities in neonatal seizures and to evaluate the clinical profile, time of onset and its relation to etiology of neonatal seizures.
Methods: A prospective observational study including neonates presenting with seizures admitted to the NICU of a tertiary level hospital, Bangalore, from December 2012 to August 2014. Detailed history and examination of baby followed by relevant investigations including biochemical parameters were done .The etiology of neonatal seizures, time of onset and its relation to etiology and the associated biochemical abnormalities were established in each case.
Results: Out of the 110 neonates studied, birth asphyxia was the commonest cause of neonatal seizures in 66 (60%) cases, followed by neonatal sepsis and metabolic disorders. Primary metabolic abnormalities occurred in 13(11.8%) cases of neonatal seizures, most common being hypoglycemia 9 (69.3%) followed by hypocalcaemia. Associated biochemical abnormalities were seen in 33 (30%) cases with hyponatremia 13 (39.3%) being most common followed by hypoglycemia. These were most often seen with Hypoxic- ischaemic-encephalopathy.
Conclusions: Biochemical abnormalities are common in neonatal seizures and often go unrecognized. These abnormalities may significantly contribute to seizure activity and hence a biochemical work up is necessary for all cases of neonatal seizures.

Keywords: Convulsions, Neonate, Hypoglycemia, Hyponatremia, Hypoxic ischemic encephalopathy

INTRODUCTION

Neonatal seizures represent the most distinctive signal of neurological disease in the newborn period. The convulsive phenomenon is clinically significant because very few are idiopathic.[1]

The incidences varies from 1.5-3.7/1000 live births in term babies and 6-12% in babies weighing <1500 gm.[2]

Neonatal seizures also differ considerably from seizures observed in older children, principally because the immature brain is less capable of propagating generalized or organized electrical discharges.[3]

It is critical to recognize neonatal seizures to determine their etiology and to treat them for 3 major reasons as following.

1. First, seizures are usually related to significant illness, sometimes requiring specific therapy.
2. Second, neonatal seizures may interfere with important supportive measures, such as alimentation and assisted respiration for associated disorders.
3. Third, experimental data give reason for concern that the seizures per se may be a cause of brain injury.

Seizures present with varying manifestations like generalized tonic, multifocal clonic and subtle activity. Therefore it is important to recognize them and treat it, as delay in recognition and treatment may lead to brain damage.[4]

The time of onset of seizure has relationship with its etiology and prognosis. For example, birth asphyxia usually presents in the first three days of life. If the baby convulses within hours of delivery, it signifies poor prognosis and brain damage.

The presence of seizure does not constitute a diagnoses but it is a symptom of an underlying central nervous system disorder due to systemic or biochemical disturbances. Biochemical disturbances occur frequently in the neonatal seizures either as an underlying cause or as an associated abnormality, in their presence it is difficult to control seizure and there is a risk of further brain damage. Among metabolic causes hypoglycaemia, hypocalcaemia, hypomagnesemia and hyponatremia are commonly seen.[5] Early recognition and treatment of these biochemical disturbances is essential for optimal management and satisfactory long term outcome.

METHODS

This prospective observational study included 110 neonates presenting with seizures admitted to the NICU of a tertiary care institute, Bangalore during the period December 2012 to August 2014. The babies satisfying the following criteria were included in the study after due consent was taken from the parents/guardians. Ethical clearance for the study was given by the hospital ethical committee.

Inclusion criteria

1. Neonates (first 28 days of life) presenting with at least one of the following clinical type of seizures:

   • Generalized tonic seizures.
   • Multifocal clonic seizures
   • Focal clonic seizures
   • Myoclonic seizures

2. Neonates with seizures who were delivered at our hospital as well as outborn babies admitted to our NICU were included in the study.

Exclusion criteria

1. Neonates with isolated subtle phenomenon, apnea or paroxysmal autonomic changes, i.e., only subtle motor moments or apnea without tachycardia were excluded from the study.
2. Jitteriness in neonates.
3. Tetanic spasms in neonates.

Detailed antenatal, natal and post natal history were taken.

History of seizures

The day of onset of seizures, type and the duration of the seizures were recorded. They were further classified according to Volpe's classification into multifocal, clonic, focal tonic, tonic and myoclonic.[6]

Examination

The vital signs of the baby were recorded. General physical examination and any disparity in head size and shape, skin lesions were noted. Gestational age was assessed according to New Ballard scoring. CNS examination was done and HIE was staged according to modified Sarnat's staging.[7] Other systems were also examined.

The following investigations were done for neonatal seizures.

- Complete blood count, sepsis screening, peripheral smear, CRP and blood culture, blood glucose. Serum electrolytes were done on emergency basis; serum calcium, serum phosphorus, serum sodium, serum potassium, serum chloride and serum magnesium were done using semi auto analyzer (by Colorimetric method)
- CSF analysis: LP was performed and CSF analysis and culture was done.
- Other metabolic screening like serum ammonia and serum lactate was done if particular metabolic disease was suspected.
- Radiological investigations: Chest X-ray and Ultrasound of cranium was done.
- CT scan or MRI brain was done as and when necessary.
- EEG was done as and when required.

Statistical methods

Descriptive and inferential statistical analyses were carried out in the present study. Results on continuous measurements are presented as Mean±SD (Min-Max) and results on categorical measurements are presented in number (%). Significance is assessed at 5% level of significance.

Statistical software

The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data.

RESULTS

Analysis of cases and results

There were 110 neonates with seizures admitted to NICU of the tertiary care hospital, Bangalore during the study period.

Gestational age and birth weight distribution

In the present study, out of 110 babies 100 were full term, of which 89 (80.9%) were AGA and 11 (10%) SGA. There were 8 (7.9%) preterm and 2 (1.89%) post term babies. 72 neonates (65.5%) were >2.5 kg, 23 (20.9%) between 2 and 2.5 kg, 15 (13.6%) between 1 and 2 kg and none <1 kg.

Sex distribution

In our study, 70 (64%) were males and 40(36%) were female babies with a male to female ratio of 1.7:1.

Type of seizures

In our study, most common seizures were subtle seizures 52 (47.3%) followed by 12 (10.9%) generalized tonic, 15 (13.6%) multifocal clonic, 21(19.1%) focal clonic, 6 (5.5%) subtle with GTS and 4 (3.6%) subtle with clonic.

Table 1: Etiology of neonatal seizures.

Etiology	No. of cases (n=110)	%
Birth asphyxia	66	60.0
Septicemia	25	22.7
Metabolic	13	11.8
ICH	2	1.8
Structural	1	0.9
Unknown	3	2.7
Total	110	100

Etiology of seizures

Birth asphyxia 66 cases (60%) was the commonest cause of neonatal seizures in our study followed by neonatal septicemia. 13 (11.8%) had pure metabolic disorders, 2 (1.8%) babies had intracranial haemorrhage, 1 baby had a structural anomaly of partial agenesis of corpus callosum. In rest 3 (2.7%) cases no cause was identified.

Day of onset of neonatal seizures

Onset of seizures on first day of life was seen in 61 neonates (55.56%).On second day and third day of life, 13 (11.8%) and 7 (6.4%) neonates developed convulsions respectively. The first three days of life together constituted the maximum (73.6%) of neonatal seizures. Late onset seizures i.e. after 8 days of life constituted 15 cases. P-value <0.001 (statistically significant) was for onset of seizure on day 1 of life.

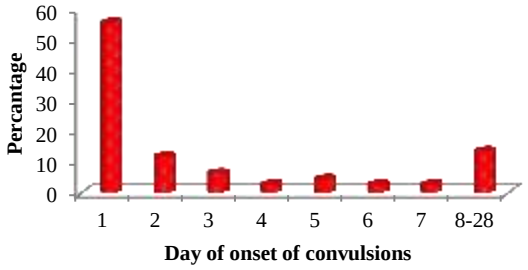

Figure 1: Day of onset of convulsions.

Correlation of etiology with day of onset of neonatal seizures

P value of <0.001 (statistically highly significant for onset of seizures on first three days of life with birth asphyxia).The onset of seizures on the first day was seen in 59 neonates out of which 54 (91.5%) were due to birth asphyxia. On the 2nd day of life ,14 babies developed seizures and 10 (71.4%) were due to birth asphyxia, two were due to hypoglycemia alone, 1 was due to hypocalcaemia and one was due to a congenital anomaly. With respect to late onset seizures (>8 days) out of 16 cases, 14(87.4%) were due to neonatal meningitis and was statistically highly significant (p value <0.001).

Overall bio-chemical profile in patients with neonatal seizures

Metabolic abnormalities were seen in 46 cases, of which 13 were purely metabolic seizures while rest of the 33 had other principal diagnoses along with metabolic abnormalities.

Overall, the most common biochemical abnormality detected in neonatal seizures was hypoglycemia in 19 (41.4%), 9 cases seen pure metabolic seizures and 10 with other non-metabolic causes.

Of the 33 cases of non-metabolic seizures, which showed biochemical abnormalities, hyponatremia was most common abnormality with 13 (39.5%) cases. 10 (47.7%) were due to HIE and 3 (30%) cases due to neonatal meningitis.

Table 2: Correlation of etiology with day of onset of neonatal seizures

Day of onset of seizures	Etiology										Total
	Birth asphxia		Metabolic				Neonatal meningitis		Others		
			Hypoglycemia		Hypocalcemia						
	No	**%**	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**	
1st	54	91.5	2	3.4	-	-	-		3	5.1	59
2nd	10	71.4	2	14.4	1	7.1	-	-	1	7.1	14
3rd	2	25.0	3	37.5	1	12.5	1	12.5	1	12.5	8
4th	-	-	-	-	-	-	2	8.0	-	-	2
5th	-	-	-	-	1	20.0	3	60.0	1	20.0	5
6th	-	-	1	33.4	-	-	2	66.6	-	-	3
7th	-	-	-	-	-	-	3	100	-	-	3
8-28	-	-	1	6.3	-	-	14	87.4	1	6.3	16
Total	66		9		3		25		7		110
P value	<0.001**		0.044*		0.020*		<0.001**		0.487		

Table 3: Overall bio-chemical profile in patients with neonatal seizures.

	Hypo Ca	Hypo Mg	Hypo Ca + Hypo Mg	Hypo Na	Hyper Mg	Hypoglycemic	Total number of patients
Metabolic Seizures	3(23.1%)	0(0%)	1(7.6%)	0(0%)	0(0%)	9(69.3%)	13(100%)
Non-Metabolic seizures	4(12.1%)	4(12.1%)	0(0%)	13(39.4%)	2(6.1%)	10(30.3%)	33(100%)
Total	7(15.2%)	4(8.7%)	1(2.2%)	13(28.2%)	2(4.3%)	19(41.4%)	46(100%)
P value	0.385	0.313	0.283	0.009**	1.000	0.022*	-

DISCUSSION

Majority of neonates with seizures in our study were full term babies and birth asphyxia was the commonest cause of seizures in these babies, similar observations were seen in a study by Moayedi AR et al and by Sandhu R et al which showed maximum cases were full term babies (81.2%) followed by preterm babies 18.8%.[8,9]

Neonatal seizures have no sex predilection. However, in our study, male to female ratio was 1.75:1.The study of neonatal seizures by Tekgul H et al, showed male to female ratio of 1.15:1.[10]

Day of onset of seizures and etiology

In our study, 61(55.5%) had onset of seizures within the first day of life and 67% were within first 48 hours of life. Kumar A et al too reported that 75% of the seizure episodes occurred before 115 hours of age and 57.8% developed seizures within the first 48 hours of life.[11] Similar findings were also published from the study by Gabriel R et al.[12]

Birth asphyxia was the most common cause of neonatal seizures in our study followed by septicemia (22.7%). Metabolic seizures were seen in 13 (11.8%) cases of which 9 cases were hypoglycemia followed by 3 cases of hypocalcemia and 1 case of combined hypocalcemia and hypomagnesemia.

Moayedi AR et al, study found that the etiology of neonatal seizures was HIE (36.4%) followed by infections (19.1%), metabolic disorders (7.3%), ICH (2.7%) and structural disorders (1.8%). In 32.7% of the cases the etiology was not identified. This study had findings similar to our study.[8]

Studies by Arun S et al, and Gabriel R et al also showed that birth asphyxia was the commonest cause of neonatal seizures followed by infections or metabolic causes.[12,13]

Biochemical profile in patients with neonatal seizures

Of the 110 neonates, biochemical abnormalities were seen in 46 cases (41.81%) of which non-metabolic seizures constituted 33 (71.7%) cases and pure metabolic seizures were seen in 13 (28.2%) cases.

Overall, the most common biochemical abnormality in our study was hypoglycemia 19 (41.4%) (p-value <0.001). While the most common biochemical

abnormality in pure metabolic seizures seen was hypoglycaemia, the most common biochemical abnormality seen in non-metabolic seizures was hyponatremia. 13 cases (39.4%) of non-metabolic seizures of which 10 (15.15%) cases of HIE and 3 (12%) cases due to neonatal meningitis demonstrated hyponatremia.

Among pure metabolic disorders 3 (23.1%) cases had hypocalcemia and one case had combined hypocalcaemia and hypomagnesemia.

HIE was also associated with hypomagnesemia in 2 (3.03%) cases, 3 (4.5%) cases of hypocalcemia and 5 (7.57%) cases of hypoglycemia.

Studies conducted by Kumar et al. and Sood A et al, also showed that biochemical abnormalities were seen in a significant number cases of HIE, intracranial bleeds and also infections which supports the findings from our study.[14]

Kumar et al, showed that hyponatremia was the most common biochemical abnormality in HIE while Sood A et al demonstrated that hypoglycemia was the commonest abnormality followed by hypocalcaemia.[14,15]

Table 4: Comparison of various studies showing metabolic seizures.

Studies	Hypo-calcemia		Hypo-magnesemia		Hypocalcemia + Hypomagnesemia		Hyponatremia		Hypoglycemia		Total
	No	%	No	%	No	%	No	%	No	%	13
Present study	3	23.1	-	-	1	7.6	-	-	9	69.3	9
Kumar et al[15]	5	55.5	1	11.1	-	-	1	11.1	5	55.5	10
Sood A et al[14]	7	70	3	30	-	-	-	-	4	40	17
Gabriel R et al[12]	-	-	-	-	5	29.4	-	-	3	17.6	21
Kumar A et al[11]	9	42.8	-	-	1	4.7	-	-	10	47.6	3
Tekgul H et al[10]	-	-	-	-	1	33.3	-	-	2	66.6	

CONCLUSION

The recognition of the etiology for the neonatal seizures is often helpful with respect to prognosis and treatment. The most common etiology for neonatal seizures is still hypoxic ischaemic encephalopathy which can be prevented if proper antenatal and perinatal care is given.

The time of onset of neonatal seizures, is significantly associated with the etiology (e.g. onset of seizures within first three days is significantly associated with birth asphyxia).

Biochemical disturbances occur frequently in neonatal seizures either as an underlying cause or as an associated abnormality. In their presence it is difficult to control seizures and there is a risk of further brain damage. Early recognition and treatment of biochemical disturbances are essential for optimal management and satisfactory long term outcome.

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