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Clinico-Biochemical Abnormalities in Hospitalized Neonates with or without Seizure

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Abstract

Introduction: *To determine the clinical types and etiological factors and to assess the biochemical abnormalities in neonates with seizure.* ***Materials and Methods:*** *This was a Cross-sectional, comparative hospital based study. Ninety neonates, age up to 28 days of both sexes were evaluated for clinical types, etiological factors and biochemical abnormalities with seizure and compared with those having no seizures. The variables were analyzed using student t- test. All the data was processed and analyzed by computer software SPSS version 15.0. Level of significance was considered as p value less than 0.05.* ***Results:*** *Most of the neonates having seizures (72%) within 3 days of life. The seizures were common in male babies (62%). 35% of the mother of baby with seizure gave history of prolonged labour. HIE was diagnosed 56.67% neonates with seizure whereas infection were found in 25% cases with seizure. Among the seizure subtypes, subtle seizures were 58% followed by clonic seizures 30%. Significant biochemical changes we found in 43.34% of neonates with seizures. Hypocalcemia (46%) was most common followed by hypoglycemia(38%).* ***Conclusion:*** *Hypoxic ischemic encephalopathy was the commonest cause of neonatal seizure followed by neonatal infections including meningitis and sepsis.. Biochemical abnormalities are more common in neonates with seizure than neonates free from seizure. Among the biochemical abnormalities hypocalcaemia and hypoglycemia occurs most commonly followed by hyponatraemia and hypomagnesaemia.*

Keywords: *Neonate, Seizure, Biochemical abnormality.*

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Introduction:

Neonatal seizures are common and may be the first manifestation of neurological dysfunction after a variety of insults[1]. Neonatal seizures are clinically significant because very few are idiopathic[1,2]. Moderate to severe acute hypoxic ischemic encephalopathy (HIE) accounts for approximately two third of all cases of neonatal seizures[3]. Biochemical disturbances occur frequently in neonatal seizures either as an underlying cause or as an associated abnormality[4,5,6]. Among the biochemical abnormalities hypocalcemia and hypoglycemia were most common showed in different studies. Hypoglycemia is common among neonates whose mothers have diabetes, large for gestational age, having HIE or other stresses[7]. Early onset (first 72 hours) hypocalcemia usually associated with preterm LBW, IUGR, asphyxia, infant of diabetic mother where as late onset hypocalcemia is seen in child fed evaporated cow's milk & other improper formulas[3,8]. About half of neonates with seizures secondary to hypocalcemia, also have hypomagnesemia and should be considered if seizures continue after given therapy[7,9]. Prognosis of neonatal seizures however is related to pathogenesis i.e. prolong or recurrent hypoglycemia permanently affect the CNS[7]. Thus early recognition and treatment of biochemical disturbances is essential for optimal management and satisfactory long term outcome[1,2]. The present study is designed to assess the biochemical abnormalities associated with neonatal seizure and to compare the findings with those of neonates having no seizures.

Materials & Methods:

The present study was a cross sectional, comparative study conducted in the department of pediatrics, Mymensingh Medical College Hospital, Mymensingh, Bangladesh from 1st July 2008 to 30th June 2009. Total 90 neonates within 28 days of life were included in the

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study. Among them 60 were with seizures and rest 30 were without seizures. Both study group and reference group were taken according to inclusion criteria and selected randomly. Seizures were diagnosed and classified by author himself or by authorized person. The neonatal seizures were classified according to Volpe's classification. Hypoglycemia were defined as blood sugar < 40 mg/dl, and hypocalcaemia when total serum calcium was < 7.0 mg/dl. Age, sex, etiological factors and biochemical parameters were recorded in a predesigned data sheet. The data was analyzed by using SPSS version 15.0.

Results:

Total 90 neonates who were admitted into neonatal unit in MMCH included in this study. Among them 60 having convulsion and rest are without convulsion. Out of 90 neonates 54 (60%) were male and 36(40%) were female. 37(61.67%) of the neonates with seizure were male. On the other hand 17(56.66%) males having no seizure among control group. Most of the seizures about 43 (71.66%) cases occurring in our study within first three days of life. In the present study 32 babies had seizure in the range of 1-15 minutes. 27 babies had seizures less than 1 minute of duration and one baby had seizure persisting more than 15 minutes. Among the mothers of neonates with seizure, 34(56.6%) suffered from different types of problems during pregnancy or labour. Twenty one (56.6%) having history of prolong labour and 5 (8.3%) having PROM. Majority about 42(70%) in neonates with seizure and 18(60%) in neonates without seizure had normal vaginal delivery and caesarian section were 16(26.6%) and 12(40%) respectively. Thirty five (58%) neonates with seizure were born in home. Most of the neonates with seizure 58(96.67%) and without seizure 27 (90%) under study were born within normal gestational period. Maximum patient under this study were born at term about 91%. About 16 (26.66%) of the neonates were fed with foods other than colostrums in neonates with seizure. Neonates were subsequently fed with breast milk in 41 cases in neonates with seizure. Hypoxic ischemic encephalopathy (HIE) was the commonest diagnosis found in 34 (56.67%) neonates with seizure group and other causes are septicemia, meningitis intracranial hemorrhage and low birth weight. No cause could be identified in 4 (6.67%) cases of neonates with seizure, out of which 3 (5%) suspected clinically due to primary metabolic disorder. Subtle types of seizure were noticed in 35 (58.33%) cases and subsequently focal or multifocal clonic were 18 (30%) and 7 (11.67%) patients had tonic type of seizures. One of them was generalized tonic convulsion. There was no myoclonic type of seizure diagnosed. 26(43.33 %) patients had eye manifestation and 16 (26.67%) patients had mouth deviation. The biochemical parameters done in the present study were the blood glucose, serum calcium, serum sodium, serum magnesium, serum potassium and serum inorganic phosphate level and to see if any significant biochemical changes in different types of seizure occurring due to different causes and it was compared with that in non-seizure neonates.

The mean serum sodium (134.8 ± 4.3 meq/L) was found to be much lower in the neonates with seizure than the neonates without seizure (139.74 ± 3.5 meq/L). The mean blood glucose level in the neonates with seizure was 2.72 ± 0.91 m mol/L which was also much lower than the other group where it was 4.18 ± 0.96 mmol/L. The neonates with seizure also had lower mean serum calcium level 7.25 ± 0.4 mg/dl which was 8.51 ± 0.72 mg/dl in case of neonates without seizure **(Table III)**.

Table-I: Values expressed as number and percentages. The total no. of significant biochemical changes are more due to multiple response i.e. multiple biochemical changes in a single case.

Table-I: Types of seizure with biochemical changes.

Seizures type	Total no of cases	Significant biochemical change	Hypoglycemia	Serum Na		Hypocalcaemia	Hypomagnesemia	Hypokalaemia	Hyperphosphatemia
				Hypo	Hyper				
Subtle	35	16 (45.71%)	5	2	0	6	2	1	0
Clonic	18	10 (55.55%)	4	0	1	4	1	0	0
Tonic	7	4 (57.14%)	1	1	0	2	0	0	0
Myo clonic	0	0	0	0	0	0	0	0	0
Total	60	26 (43.33%)	10 (38.4%)	3 (11.5%)	1 (3.8%)	12 (46.1%)	3 (11.5%)	1 (3.8%)	0

Fig 1: Hypoxic ischemic encephalopathy (HIE) was the commonest diagnosis was found in 56.67% neonates with seizure group. Infection in the form of septicemia and meningitis were found in 25% cases with seizure.

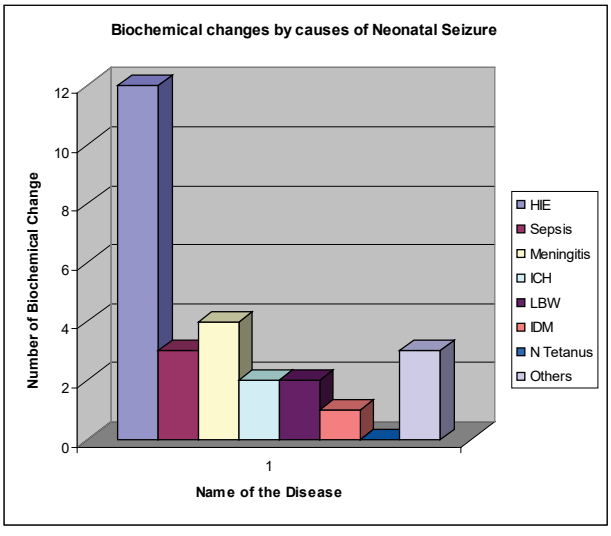

Figure-1: Clinical diagnosis of the neonates with seizur.

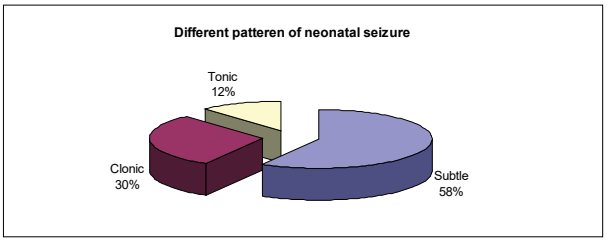

Figure-2: Types of seizure among Study group (n=60).

Table II. shows hypocalcemia and hypoglycemia were more common in neonates with seizure where as hypoglycemia and hyponatraemia were found in neonates without seizure.

Table-II: Distribution of seizure and non seizure neonates with biochemical changes.

Biochemical parameters	Neonates with Seizures (n=60)	Neonates without Seizures (n=30)
Hypoglycemia	10 (16.67%)	1 (3.34%)
Hypocalcaemia	12 (20%)	0
Hypomagnesaemia	3 (5%)	0
Hyponatraemia	3 (5%)	1 (3.34%)
Hypernatraemia	1 (1.67%)	0
Hypokalaemia	1 (1.67%)	0
Hyperphosphatemia	0	0

Table III: Statistical T-test was done to see if there is any statistically significant difference in the biochemical levels of the neonates with seizure and no seizure. Statistically significant difference ($p < 0.001$) was found in cases of Blood glucose, Serum calcium, Serum sodium and Serum magnesium level between the two groups.

Table-III: T-test: Neonates with seizure and no seizure by biochemical changes.

Biochemical parameters	Seizure	Number	Mean	SD	T-value	P-value
Blood Glucose	Yes	60	2.72	.91	7.02	< .001
(m mol/L)	No	30	4.18	.96		
Serum Sodium	Yes	60	134.8	4.3	5.3	< .001
(meq/L)	No	30	139.74	3.5		
Serum Calcium	Yes	60	7.25	.40	10.4	< .001
(mg/dl)	No	30	8.51	.72		
Serum Potassium	Yes	60	4.28	.68	.79	>.05
(meq/L)	No	30	4.4	.66		
Serum Magnesium	Yes	60	1.91	.35	3.5	< .001
(mg/dl)	No	30	2.35	.29		
Serum Phosphate	Yes	60	2.1	.33	.88	>.05
(mmol/L)	No	30	2.03	.40		

Discussion:

Neonatal seizure is an acute emergency which is responsible for very high morbidity and mortality[10,11]. Neonatal seizure observed more in male patient (61.67%) than female (38.33%) in this study which is consistent with study done by Taksande AM et al[10] showed 66.4% male and 33.6% in female newborn. Shah et al[11] also found male predominant in neonatal seizure. The most common seizure type in term and preterm babies is the subtle seizure[12,13]. In this study, majority of the patients (58.33%) showed subtle type of seizure whereas clonic and tonic seizures were 30% and 11.67% respectively. Ross et al[14] showed 40.6% subtle, 35.59% clonic, 8.9% generalized tonic and 27.78% myoclonic type of seizures. Soni A et al[15] reported 25% subtle and 37.5% tonic seizures and Taksande AM et al[10] showed 31.1% subtle and 46.7% clonic seizures in term babies whereas 48.4% had subtle and 27.2% had clonic seizures in preterm babies and tonic seizures observed in 19.4% and 24.2% in term and preterm babies respectively. Shah et al[11] reported 42.2% subtle, 44.4% clonic, 11.1% tonic and 2.2% myoclonic seizures in a observational study conducted in Nepal.

Coen RW et al[16] found 81% of babies had early onset seizures (< 72 hrs). Ross AL et al[14] and Taksande AM et al[10] also found early onset seizures in 50.33% and 85.45% babies respectively whereas in this study we found 71.66% neonates had seizures within 72 hrs. Brown JK et al[17] observed 43% neonates had seizures in the first 4 days of life while Ronen GM et al[18] reported 83% seizures in the first week of the life.

The etiology of neonatal seizure is not disease specific and may be due to a combination of abnormalities[4]. The most common cause of seizure encountered in this study was birth asphyxia, occurred in 34 (56.67%) cases. Sood et al,[4] Kumar et al,[5] and Shah et al[11] reported birth asphyxia as etiology of seizure was 45.71%, 48.27% and 44% cases respectively which are comparable with the result of present study. Similar observation seen by Mizrahi where HIE as the cause of convulsion in 46% cases[19]. Taksande AM et al[10] reported 42.7% and Brown et al[17] showed 65% cases of neonates of perinatal asphyxia experienced with seizure. Eriksson M et al,[20] Painter MJ et al [21] and Holden KR[22] et al also showed similar results.

Sepsis in neonate is often associated with meningitis and is a cause of significant morbidity and mortality[12]. A study conducted by Legido A et al[23] reported 5% septicemia and 12.25% meningitis. Ross et al[14] showed 9.5% babies had septicemia. Shah et al[11] and Taksande AM et al[10] both of the study reported about 20% cases suffered from infection; sepsis and meningitis combined. These results are concordance with our study where sepsis were diagnosed in 13.33% cases and meningitis in 11.67% cases of neonates with seizure. Preterm babies are more vulnerable to intraventricular hemorrhage either spontaneously or as a result of Perinatal asphyxia[13]. Taksande AM et al[10] showed 1.29% term neonate and 18.18% preterm neonate had IVH whereas Ross et al[14] and Scher MS et al[24] also reported higher incidence of IVH in preterm babies which are comparable with present study where we found out of three neonates (5%) having IVH which were diagnosed clinically and one of them were preterm.

The incidence of primary metabolic cause of convulsion is about 10%[12]. In this study, 4 (6.67%) cases no other cause of seizure could be detected. Out of them 3 (5%) were clinically suspected as primary metabolic disorder. One of them was hypoglycemic and other two cases showed significant hypocalcaemia. Hypomagnesaemia was associated with one of the hypocalcemic baby. Kumar et al shown primary metabolic disorder accounted 25.7% causes of seizure[5]. This is in contrast to report from western countries where improvements in infant feeding practices have made this category an uncommon cause of seizures[8]. In a study by Cockburn et al it was found that 55% of neonatal seizures were due to primary disturbance of mineral metabolism[6].

Hypocalcaemia was the most common biochemical abnormalities among 12(46.15%) neonates in this study (Table I)

similar to the study done by Sood et al[4] about 48.27% and Kumar et al[5] about 31.8% cases. Hypoglycemia was the second most common biochemical abnormalities found in 38.46% cases which similar to Sood et al[4] and Kumar et al[5] where values were 48.27% and 50% respectively. Shah et al[11] reported 22% whereas Taksande et al[10] experienced only 8.1% of hypoglycemia in neonatal seizures. Three (11.53%) neonates with seizure present with hyponatraemia and 1 (3.84%) with hypernatraemia, 1(3.84%) with hypokalaemia and 3(11.53%) with hypomagnesaemia which is comparable with study done by Sood et al[4] and Kumar et al[5] where reported 17.24% and 45.45% cases of hyponatraemia respectively. Hypernatraemia and hypokalaemia we found was associated with HIE. Two baby of hypomagnesaemia were associated perinatal asphyxia and one was suspected primary metabolic disorder. Two cases were associated with hypocalcaemia. Kumar et al found hypomagnesaemia in 9% case of neonatal seizures[5] which is consistent with our study.

Biochemical changes we found 6.67% cases of neonates without seizures and 43.33% neonates with seizures. Among these non-seizure cases, one (3.3%) was hyponatraemic diagnosed as a case of birth asphyxia and another one was hypoglycemic diagnosed as neonatal sepsis. The biochemical changes found in the non-seizure neonates may be attributed to the disease conditions with which the neonates were admitted to the hospital. The mean of all the biochemical parameters except serum phosphate were found to be higher (within normal range) in the non-seizure cases. The difference in the mean value of glucose, calcium, magnesium and sodium between the two groups was found to be statistically significant ($p < 0.001$).

In this study, though individual variation in respect of race, geography and socioeconomic condition are present even then most of the study findings are consistent with that done in abroad.

Conclusion:

Perinatal asphyxia leading to Hypoxic ischemic encephalopathy was the commonest cause of neonatal seizure followed by neonatal infections including meningitis and sepsis. Most seizures occurred within first 72 hours of postnatal age. Meningitis mostly occurs after first week of life. Subtle seizure was the commonest type of seizure that can easily missed, as it is very mild. Biochemical abnormalities are more common in neonates with seizure than neonates free from seizure. Among the biochemical abnormalities hypocalcaemia and hypoglycemia occurs most commonly followed by hyponatraemia and hypomagnesaemia.

Conflict of Interest: None.

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