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ORIGINAL ARTICLE

Spectrum of Biochemical Abnormalities in Neonatal Seizures: A Cross-sectional Study in A Tertiary Care Paediatric Hospital

Sultana Yeasmin[1], ASM Nawshad Uddin Ahmed[2]

Abstract

Background: *Neonatal seizure by itself is not a diagnosis but is a manifestation of an underlying disease of central nervous system which may result due to systemic and biochemical abnormalities. Biochemical disturbances are transient and rapidly correctable. This study aims to assess biochemical abnormalities in neonatal seizure.*

Objective: *Aims of the study were to describe biochemical abnormalities in neonatal seizure.*

Methods: *This cross-sectional study has been conducted in the Department of Paediatrics, Bangladesh Shishu Hospital & Institute from January to July 2020. Neonates admitted with history of convulsion or who developed convulsion during hospitalization were included and neonates having congenital malformation of brain, syndromic baby were excluded from this study. Baseline characteristics of neonates including sex, gestational age, weight, head circumference, details of seizure including age at onset, duration, number, and type were recorded. Blood glucose, serum calcium, sodium, potassium, and magnesium level were done immediate after admission before instituting any specific treatment. Informed verbal consent from caregiver was taken before enrolment.*

Results: *Total 60 neonates presenting with seizure were enrolled in the study. About two-third neonates presented with generalized tonic clonic seizure (43/71.7%). Majority (51/85%) of the neonates had seizure within 72 hours, rest of them after 72 hours. Out of 60, 32(53.3%) neonates had biochemical abnormalities of which 28(87.5%) were non-metabolic and 4(12.5%) were primary metabolic seizures. Hypoglycaemia and hypocalcaemia were equally found in primary metabolic seizure. Non-metabolic seizures were associated with perinatal asphyxia, meningitis, sepsis, and intracranial haemorrhage. Hypoglycaemia (67.8%) was commonest abnormality among secondary causes, followed by hyponatremia (21.4%) and hypocalcaemia (10.7%). Among 32 cases, 66.67% hypoglycaemia and 50% hyponatremia were found in perinatal asphyxia cases, which was higher than other cases.*

Conclusion: *This study showed hypoglycaemia was commonest abnormality among biochemical changes in neonatal seizure. Hypoglycaemia and hyponatremia occur with higher frequency in case of perinatal asphyxia.*

Keywords: *Neonatal seizure, hypoglycaemia, hyponatremia, hypocalcaemia.*

1. Registrar, Paediatric Endocrine and Metabolic Disorder, Bangladesh Shishu Hospital & Institute.
2. Professor of Paediatric Endocrine and Metabolic Disorder, Bangladesh Shishu Hospital & Institute.

Correspondence to: Dr. Sultana Yeasmin, Registrar, Paediatric Endocrine and Metabolic Disorder, Bangladesh Shishu Hospital & Institute, Sher-e-Bangla Nagar, Dhaka-1207. Cell: 01752-871019, E-mail: sultanayeasmin102@gmail.com

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Introduction

Seizure is the most common and distinct sign of neurological dysfunction in neonates. Neonatal seizures are abnormal electrical discharge in the central nervous system of neonates, usually manifesting as stereotyped muscular activity or automatic changes.[1] Seizures occur when a large group of neurons undergo excessive synchronized depolarization, which can result from excitatory amino acid release or deficient inhibitory neurotransmitter. Another potential cause is disruption of ATP dependent resting membrane potentials, which causes a flow of sodium into the neurons and potassium out of the neurons.[2] It may manifest as impairment or loss of consciousness, abnormal motor activity, behavioural abnormalities, sensory disturbances, or autonomic dysfunction.[3]

Neonatal seizures are clinically significant as they may be symptomatic of an underlying disorder or primary epileptic condition. The occurrence of seizure may be the first indication of neurological disorder and the time of onset of seizure has relationship with the aetiology of seizure and prognosis.[4] Neonatal seizure may arise as a result of diverse aetiologies and can have varied presentation.[5] The major causes of neonatal seizures are perinatal asphyxia, metabolic abnormalities (hypoglycaemia, hypocalcaemia, hypomagnesemia, pyridoxine dependency and deficiency, hyponatremia and hypernatremia, amino aciduria and kernicterus), infection (sepsis, meningitis and encephalitis), bleeding (subarachnoid, subdural, thrombosis and intraventricular haemorrhage), developmental anomalies (cerebral dysgenesis, incontinentia pigmenti) and other causes (drug withdrawal), hyperthermia, benign familial neonatal seizure, benign idiopathic neonatal seizures and benign sleep myoclonus.[6-8] Among various aetiologies perinatal asphyxia, sepsis, neonatal meningitis and metabolic abnormalities are commonest aetiologies of neonatal seizures.[3]

Biochemical disturbances occur frequently in neonatal seizure either as an underlying cause or as associated abnormalities. In their presence it is difficult to control seizure and there is a risk of further brain damage.[4,9] So early recognition and treatment of those aetiologies are essential for optimal management and satisfactory long-term outcome.[9] Aims of the study were to describe clinical presentation, time of onset of seizure and to determine biochemical abnormalities in neonatal seizure.

Materials and Methods

This was a cross-sectional study, conducted in the Department of Paediatrics at Bangladesh Shishu Hospital & Institute, Sher-e-Bangla Nagar, Dhaka-1207, from January to July 2020. Neonates (0-28 days) admitted in Department of Paediatrics with history of convulsion or who developed convulsion during hospitalization were included and neonates having congenital malformation of brain, syndromic baby, whose caregiver did not give consent were excluded from this study. Informed verbal consent from caregiver was taken before enrolment. Data was collected by structured questionnaire with maintaining proper ethical issues.

Baseline characteristics of patient, clinical details of seizure including age of onset of seizure, duration, frequency, type of seizure were recorded. Before instituting treatment, 2ml blood drawn from median cubital vein for blood sugar, serum calcium, sodium, potassium, chloride, magnesium and was sent to Biochemistry department for analysis. Report was collected from patients hospital record. Criteria for diagnosing biochemical abnormalities are - Hypoglycaemia: Blood glucose level <40mg /dl (2.2 mmol/L), Hypocalcaemia: Total serum calcium <7 mg / dl (1.75 mmol/L) or ionized calcium <4 mg /dl (1 mmol /L), Hypomagnesaemia: Serum magnesium level <1.5 mg/dl, Hyponatremia: Serum sodium level <130 meq/dl, Hypernatremia: Serum sodium level >150 meq/dl. Data were processed and analysed by using SPSS (statistical package for social sciences) version-23. Data was described as percentage.

Results

Out of 60 neonates, 41 (68.3%) were males and 19 (31.7%) females; male to female ratio of 2.16:1. Forty-four neonates were full-term (90%), 6 were preterm (10%). Fifty-two cases (86.7%) were appropriate for gestational age (AGA) and 8 (13.3%) were small for gestational age (SGA) (Table I).

In present study 85% (51/60) neonates had seizure within 72 hours of life, among them 36.7% (22/60) neonates had seizure on first day, 38.3% (23/60) on second day and 10% (6/60) on day 3; and after 72 hours of life, 15% (9/60) neonates had seizure (Fig.-1). Generalized tonic seizure was the commonest type of seizure (43, 71.7%); followed by focal (10, 16.6%),

subtle (5, 8.3%), myoclonic (1, 1.7%) and partial (1, 1.7%) seizure (Table II). Perinatal asphyxia (60%) was most common cause of neonatal seizure; followed by meningitis (16.7%), sepsis (15%), primary metabolic causes (6.7%) and intracranial haemorrhage (1.6%) (Fig.-2). Perinatal asphyxia (68.6%) was most common cause of seizure within 72 hours and after 72 hours meningitis was the predominant cause.

In present study, biochemical abnormalities were seen in 32 (53.3%) cases of which 28 (87.5%) were non-metabolic and 4(12.5%) were metabolic seizures. The most common type of biochemical abnormality was hypoglycaemia (65.6%) followed by hyponatremia (18.7%) and hypocalcaemia (15.6%). Among non-metabolic seizures (28, 87.5%), hypoglycaemia (19, 67.8%) was commonest abnormality; followed by hyponatremia (6, 21.4%) and hypocalcaemia (3, 10.7%). One or more abnormalities co-existed in non-metabolic seizure, those were hypoglycaemia and hyponatremia (2, 7%) and hyponatremia and hypocalcaemia (1, 3.6%). Among metabolic seizure (4), 2 cases were hypoglycaemia and 2 cases hypocalcaemia (Table III). One case of hypoglycaemia was IDM and both hypocalcaemia cases had early onset seizure; and one case was SGA and one IDM. Non-metabolic abnormalities were due to perinatal asphyxia, meningitis, sepsis, and intracranial haemorrhage, among them perinatal asphyxia was highest (18/28, 64.3%) (Table IV). Among 32 cases, 66.67% hypoglycaemia and 50% hyponatremia were found in perinatal asphyxia cases, which was higher than other cases.

Table I
Distribution of presenting characteristics of the enrolled neonates (N=60)

Characteristics		Number	Percentage
Gender	Male	41	68.3
	Female	19	31.7
Gestational age	Term	54	90.0
	Preterm	6	10.0
Weight for	AGA	52	86.7
gestational age	SGA	8	13.3

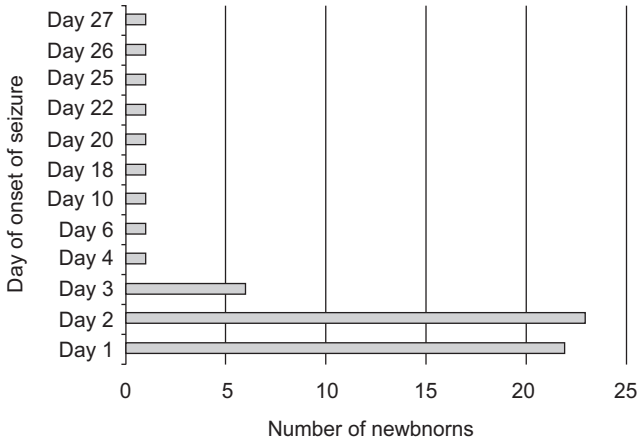

Fig.-1 *Age of onset of seizure*

Table II
Distribution of Seizure characteristics (N=60)

Seizure type	Number	Percentage
Generalized tonic	43	71.7
Focal	10	16.6
Subtle	5	8.3
Myoclonic	1	1.7
Partial	1	1.7
Total	60	100

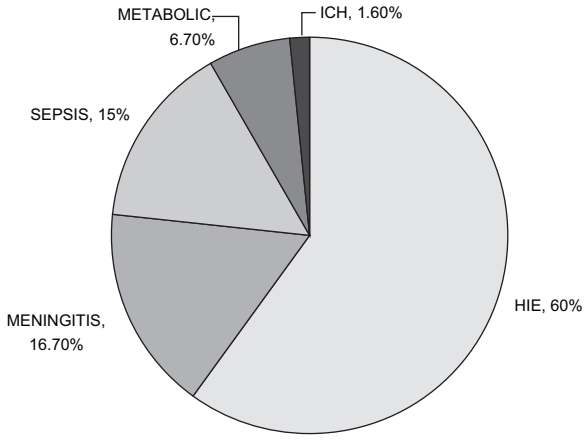

Fig.-2 *Distribution of aetiology of neonatal seizure*

Table III
Overall biochemical profile in patients with neonatal seizure (N=32)

	Number (percentage)	Hypo-glycaemia	Hypo-natraemia	Hypo-calcaemia	Hypo-magnesaemia	Hypoglycaemia+ hyponatraemia	Hyponatremia+ hypocalcaemia
Non-metabolic	28(87.5)	19(67.8)	6(21.4)	3(10.7)	0	2(7.1)	1(3.6)
Primary metabolic	4(12.4)	2(50)	0	2(50)	0	0	0
Total	32(53.3)	21(65.6)	6(18.7)	5(15.6)	0	2(6.2)	1(3.1)

Table IV
Distribution of patient of non-metabolic seizure in accordance with Biochemical profile

Etiology	Number having abnormality	Hypogly caemia	Hypo Na+	Hypo Ca++	Hypo Mg++	Hypoglycaemia and Hypo Na+	Hypo Ca++ and Hypo Na+
Perinatal asphyxia (36)	18	14	3	1	0		1
Meningitis (10)	6	4	1	1	0	1	
Sepsis (9)	3	1	1	1	0	1	
Intracranial haemorrhage (1)	1	0	1	0	0		
Total	28	19	6	3	0	2	1

Discussion

Neonatal seizures have always been a topic of interest because of their universal occurrence. The presence of a seizure does not constitute a diagnosis, but it is a symptom of underlying CNS disorder due to systemic or biochemical disturbances.[10]

In present study out of 60 neonates 41 (68.3%) were male and 19 (31.7%) were female. Male to female ratio was 2.16:1, which is similar to the study conducted by Arunkumar et al[11] (1.4:1). Mishra et al[12] also showed male predominance (1.8:1). Male predominance may be due to health care seeking behaviour for male babies in our society.

This study showed 86.7% neonate having seizure were appropriate for gestational age and 13.33% constituted low birth weight, which is similar to the study done by Das et al[4], showed AGA (81.7%), SGA (9.6%). More number of neonatal seizures having birth weight ≥2500gm may be due to perinatal asphyxia is more common in these neonates.

In this study term babies were 90% while preterm babies were 10% of all new-born's having seizure. The majorities of neonates who developed seizure were full term (90%) which is similar to the findings of Marzoki et al[2] (95.4%) and Das et al[4] (91.3%).

In our study 85% neonates had seizure within 72 hours which is similar to the study conducted by Aziz et al[5] (83%), Das et al[4] (71.3%). But Marzoki et al[2] found most of seizure occur after 72 hours. This difference may be due to aetiology. In our study perinatal asphyxia was the main cause of seizure but in the study of Marzoki et al[2] metabolic abnormalities (47.7%) were most common cause of seizure.

Generalized tonic seizure (71.7%) was predominant seizure in the present study, but Aziz et al[5] found focal clonic seizure (30%) and Das et al[4] showed subtle seizure (49%) as the commonest seizure type.

The results of the present study showed biochemical abnormalities in 53.3% of neonates with seizure which corroborated with the findings published by Aziz et al[5]. On the other hand, Arunkumar et al[11] and Kumar et al[13] found biochemical abnormalities in 82% and 62.8% neonates respectively, which was higher than our study.

We found hypoglycaemia was the principal cause of seizure (65.6%) in neonates, similarly Kumar et al[13], Arunkumar et al[11] and Aziz et al[5] found hypoglycaemia (50%, 53.6% and 50% respectively) in neonates with seizure.

In present study hyponatremia was the second most common abnormality (18.7%, 6/32) of neonates with seizure which was similar to the study conducted by Aziz et al[5] (18.5%, 10/54), Sood et al[14] (17.2% 5/29) but was lower compared to the study conducted by Kumar et al[13] (45.4%, 10/22).

This study found perinatal asphyxia accounted for 50% (3/6) of case with hyponatremia which was similar to the findings of Arunkumar et al[11] (12/24), The most probable explanation for occurrence of hyponatremia might be due to fluid overload as a result of renal compromise or due to syndrome of inappropriate secretion of antidiuretic hormone.

Hypocalcaemia was seen in 15.6% (5/32) cases in the present study, which was lower in contrary to the study conducted by Aziz et al[15] (48.1%), Sood et al[14] (48.3%), and Kumar et al[13] (31.8%).

We found primary metabolic abnormalities in 12.4% neonates due to hypoglycaemia and hypocalcaemia. Aziz et al[15] and Sood et al[14] described higher percentage (31.8%, 34.4% respectively) of primary metabolic seizure in contrary to our study. This study found primary metabolic seizure due to hypoglycaemia and hypocalcaemia, similarly found by Sood et al[14] but Aziz et al[15] found primary metabolic seizures due to hypocalcaemia, hypomagnesemia and hyperphosphatemia.

Conclusion

Among biochemical abnormalities hypoglycaemia was commonest abnormality. Hypoglycaemia and hypocalcaemia were equally observed among primary metabolic cases. Hypoglycaemia and hyponatremia occur with higher frequency in case of perinatal asphyxia. So, if biochemical correction is possible in time, we would be able to control seizure promptly.

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