



**ORIGINAL ARTICLE**

**Biochemical Changes in Neonates with and without Seizure: A Comparative Study**

ASM Shahidullah<sup>1</sup>, Rafika Afrose<sup>2</sup>, Kalpona Deb<sup>3</sup>, Bina Sen<sup>4</sup>, Arup Ratan Paul<sup>5</sup>, Kamona Rani Saha<sup>6</sup>, Nilufar Begum<sup>7</sup>

<sup>1</sup>Professor, Department of Biochemistry, Community Based Medical College, Mymensingh, Bangladesh; <sup>2</sup>Associate Professor, Department of Pharmacology, Community Based Medical College, Mymensingh, Bangladesh; <sup>3</sup>Professor, Department of Biochemistry, Mymensingh Medical College, Mymensingh, Bangladesh; <sup>4</sup>Professor, Department of Biochemistry, Community Based Medical College Bangladesh, Mymensingh, Bangladesh; <sup>5</sup>Associate Professor, Department of Biochemistry, Community Based Medical College Bangladesh, Mymensingh, Bangladesh; <sup>6</sup>Associate Professor, Department of Biochemistry, Community Based Medical College Bangladesh, Mymensingh, Bangladesh; <sup>7</sup>Associate Professor, Department of Blood transfusion Medicine, Community Based Medical College Bangladesh, Mymensingh, Bangladesh

[Received on: 1 November 2020; Accepted on: 20 December 2020; Published on: 1 January 2021]

**Abstract**

**Background:** Seizure is a common neurological disorder in the pediatric age group. **Objective:** Neonates with seizure have decreased in serum calcium, magnesium, sodium, potassium, and glucose if compared to neonates without seizure. **Methodology:** This comparative cross-sectional study was carried out in the Department of Biochemistry at Mymensingh Medical Collage, Mymensingh, Bangladesh in cooperation with the Department of Pediatric of Mymensingh Medical Collage & Hospital, Mymensingh, Bangladesh from July 2005 to June 2006. Neonates were included in the study. Subjects were divided into two groups designated as group I as control group and group II cases. From each subject at least 2 ml of blood were collected from femoral vein and was collected serum for biochemical analysis. **Result:** A total of 60 neonates were included in the study. Subjects were divided into two groups-group-I control- (n=20) and group II cases-(n=40). The concentration of serum calcium, magnesium, sodium, potassium, and glucose yielded 7.33±0.79, 5.79±1.10; 2.18±0.23,1.61±0.25; 134.82±3.03, 133.68±8.57; 4.80±0.56,5.89±2.02; 66.33±8.23, 62.25±7.96 in group I and group II respectively. **Conclusion:** Significant decreases of serum calcium, magnesium and significant increase of serum potassium in neonates with seizure are found in this study. [*Journal of Current and Advance Medical Research, January 2021;8(1):25-29*]

**Keywords:** Calcium; magnesium; sodium, potassium; glucose; neonates; seizure

**Correspondence:** Dr. ASM Shahidullah, Professor, Department of Biochemistry, Community Based Medical College, Mymensingh, Bangladesh; **Email:** shahidj3.bd@gmail.com; **Cell no.:** +8801711243018

**Cite this article as:** Shahidullah ASM, Afrose R, Deb K, Sen B, Paul AR, Saha KR, Begum N. Biochemical changes in Neonates with and without Seizure: A Comparative Study. J Curr Adv Med Res 2021;8(1):25-29

**Funding:** This study has been performed without any funding from outside else.

**Conflict of Interest:** There was no conflict of interest to any of the authors.

**Contributions to authors:** Shahidullah ASM, Afrose R, Deb K, have contributed in protocol preparation, data collection, data analysis up to the report writing; Sen B, Paul AR, Saha KR, Begum N have written & revised the manuscript.

**Copyright:** ©2021. Shahidullah et al. Published by Journal of Current and Advance Medical Research. This article is published under the Creative Commons CC BY-NC License (<https://creativecommons.org/licenses/by-nc/4.0/>). This license permits use, distribution and reproduction in any medium, provided the original work is properly cited, and is not used for commercial purposes.

## Introduction

Seizure is a common neurologic disorder in the pediatric age group. A seizure is defined as a paroxysmal involuntary disturbance of consciousness, function that may manifest as an impairment or loss of consciousness, abnormal motor activity, behavioral abnormalities, sensory disturbances or autonomic dysfunction<sup>1</sup>. Seizure is a relatively common disorder and is more recurrent in neonatal period.

The neonatal is at particular risk for the development of seizures, because metabolic, toxic, structural and infectious diseases are more likely to manifest during this time than at any other period of life. Neonatal seizures are dissimilar to those in a child or adult because generalized tonic clonic seizure do not usually occur during the first month of life as newborn infant are less able to sustain organized generalized epileptic discharge due to less organization and maturation of CNS<sup>2</sup>.

Neonatal seizures represent a major manifestation of significant neurologic disease in the newborn. It indicates CNS insult symptoms as well as a cause of brain damage. The preterm infants are more prone to develop seizure than term babies and it is more likely to be recurrent. Seizures are more frequent on the first day of life than at any other time, although the diagnosis is easily missed because their manifestations can be extremely subtle. Subtle seizures were the most common type seen in the several surveys, occurring in 75.0% of the cases described by Scher et al<sup>3</sup> Repetitive lip smacking, cycling or swimming movements, deviation of eye and apnea, which are manifestations of subtle seizures, are sometimes difficult to distinguish from normal movements of neonates.

The incidence of seizures in term babies is reported to be between 3 to 6 per 1000 live births. The incidence of clinically diagnosed seizure in very low birth weight infants varies from 50 to 60 per 1000 deliveries<sup>4</sup>. As many as 20.0% newborn in intensive care unit may have seizures activity at some time<sup>5</sup>. The overall prevalence is as low as 0.5% in term and as high as 21.0% in preterm babies<sup>6-3</sup>. The incidence also varies from place to place, as it is likely to be higher in developing countries like Bangladesh where perinatal asphyxia, prematurity and infection are high.

Seizures during neonatal period frequently create problems in diagnosis due to diversity of their

etiology as well as natures. It is often difficult to find out the cause of seizure by seeing the nature or pattern of seizure. The causes of neonatal seizures include asphyxia, birth trauma, hypoglycemia or hypocalcaemia and a few apparent causes. The onset of seizure within first 1 to 2 days considered as first peak usually is due to birth asphyxia, birth trauma and drug withdrawal. There is a second peak incidence from about 3 days and onwards which is usually due to infections and metabolic causes.

Biochemical disturbances occur frequently in the neonatal seizures, either as an underlying cause or as an associated abnormality. Early diagnosis and appropriate treatment of the biochemical abnormalities accompanying neonatal seizures is very important for effective seizure control and for avoidance of further brain damage<sup>2</sup>. Hypoglycemia is seen in 1-3 per 1000 newborn infants. Infants of diabetic mother, premature baby, and small for gestational age infants are more prone to develop hypoglycemia. Hypoglycemia may be secondary to perinatal stresses such as asphyxia, infection or respiratory distresses<sup>7</sup> during or after birth and also due to improper feeding after birth<sup>9</sup>. The etiology of hypocalcemia varies with time of onset and associated illness. It may occur in premature infants and infants of diabetic mother and IUGR babies.

Hypomagnesemia may be seen simultaneously with hypocalcemia especially in infants of diabetic mother<sup>8</sup>. Hyponatremia may result from faulty preparation of infant formulas. A low serum sodium level is thought to be a result of redistribution of total body sodium, which may be associated with severe illness and SIADH<sup>1</sup>. Neonatal seizure is one of pediatric emergencies and mostly requires hospitalization. Early diagnosis, prompt investigation for detecting the cause and urgent treatment with anticonvulsants are of critical importance. Recognition and diagnosis may uncover the underlying process, which may require specific therapy in addition to seizure control. Delayed recognition of treatable causes, like hypoglycemia may have profound effect on outcome. Secondly seizure may interfere with cardio respiratory function. The present study was designed to assess the biochemical abnormalities associated with neonatal seizure and to compare the findings with those of neonates without seizure.

## Methodology

This was comparative cross sectional study. The study was carried out in the Department of Biochemistry, Mymensingh Medical College in cooperation with pediatric department of

Mymensingh Medical College and Hospital, Mymensingh, Bangladesh. In the present study, neonates were included. Subjects were divided into two groups designated as Group I (n =20) and group II (n =40). In group B neonates were without seizure and were forty neonates with seizure, admitted in the pediatric department of Mymensingh Medical College and Hospital were included in the study groups. The inclusion criteria for cases (group II) were neonates admitted in Mymensingh Medical Collage Hospital with seizure, age of 0-28 days and either sex with seizure. The exclusion criteria for cases of group II were neonates with jitteriness, neonate with major congenital anomalies, tetanus neonatorum and neonates with seizure who already received medication with glucose and calcium. Data were collected through a preformed data collection sheet (questionnaire). The guardians of the subjects were informed about the nature and purpose of the study. Blood sample was collected and questionnaire was filled up. Finally, the subjects of this study were included on the basis of exclusion & inclusion criteria. Blood samples were collected in neonates with seizure before any kind of infusion or drugs were administered from admitted subjects with all aseptic precautions. From each subjects at least 2 ml of blood were collected from femoral vein. The collected blood was transferred to a dry screw capped test tube immediately after removal of needle from the nozzle. The blood was poured in a linear stream along the side of the tube by a gentle push of the piston. Test tubes were kept in standing position until clot formation. Then the test tubes were centrifuged at 3000 rpm for 30 minutes. The sera obtained by centrifuging were kept in Eppendorf's after proper labeling. Experiments were carried out as soon as possible after sampling. Whenever there was delay in experiments, samples were stored by refrigeration at -10 to -15<sup>0</sup> C prior to the analysis, for a maximum of 10 days. Serum calcium, magnesium and glucose were determined in the laboratory by Photometric principle using recommended commercial kit. For electrolytes: Ion selective electrode method (ISE): Auto calibrated by electrolyte analyzer with ISE method. Analysis of different concentration of standard solution of serum calcium, magnesium, and glucose were performed to obtain a calibration chart. Statistical significance of the difference between the mean values of the parameters estimated were evaluated by unpaired 't' test.

**Result**

Serum calcium, magnesium, sodium, potassium and glucose were estimated in 60 subjects divided in to

group I (control n=20) and group II (neonates with seizure, n=40). Serum calcium, magnesium and glucose were expressed in mg/dl and, sodium, potassium were expressed in mEq/L.

**Table 1: Comparison of Mean Serum Calcium, Magnesium, Sodium, Potassium and Glucose in the Study Subjects (Mean ± SD)**

Variables	Group I	Group II	P value
S. Ca	7.3±0.79	5.8±1.10	0.001
S. Mg	2.2±0.23	1.6±0.25	0.001
S. Na	134.8±3.03	133.7±8.57	0.452
S. K	4.8±0.56	5.9±2.02	0.05
S Glucose	66.3±8.23	62.3±7.96	>0.05

Group-I = Control Group, Group-II = Study case, SD = Standard Deviation; S.=Serum

**Discussion**

In the present case control study an attempt was made to assess the biochemical changes (serum, calcium, magnesium, sodium, potassium and glucose) that are associated with neonates with seizures by comparing these biochemical parameters with the findings in neonates without seizure. Study was conducted in the neonatal unit of Mymensingh Medical College Hospital. The control group comprised of healthy children without seizure. We excluded those neonates who developed seizure after infusion of any kind of fluid, because infusion fluid could alter the biochemical changes. Mean values of serum calcium yielded 7.33 ±0.79 and 5.79 ±1.10 in group I and group II respectively in the present study. Serum calcium decreased significantly (P<. 001) in-group II (Cases) in comparison to group I (Control). The findings were comparable to studies carried out by<sup>2-9-11</sup>.

In this case control study serum calcium, magnesium, sodium, potassium and glucose level were studied on 60 neonates from neonatal unit and Obstetrics Ward of Mymensingh Medical College. Out of 60 subjects 20 were taken as control on the basis of no history of convulsion. Another 40 neonates were selected as cases on the basis of convulsion. Cases were selected from Department of Pediatrics at Mymensingh Medical College. Subjects were classified in two groups. Group I (n=20) - control, group ii (n=40) cases. Finally, 60 samples of blood (20 from control and 40 from cases) were subjected to estimation of serum calcium, magnesium, sodium, potassium and glucose.

Hypocalcemia is common in sick infants due to high levels of PTH antagonist like glucocorticoid and calcitonin. In the study mean values of serum magnesium yielded  $2.18 \pm 0.23$  and  $1.61 \pm 0.25$  in group I and group II respectively. Mean serum magnesium showed significant difference between group I and group II ( $P < 0.001$ ). Serum magnesium decreased in-group II (Cases) in comparison to group I (Controls). Kumar, Sood and their associates have found hypomagnesemia which are consistent with the present study<sup>9, 2</sup>.

Hypocalcaemia and hypokalemia may not respond to supplementation if concurrent hypomagnesemia is incorrect. In the present study mean values of serum sodium yielded  $134.82 \pm 3.03$  and  $133.68 \pm 8.57$  in group I and group II respectively. There was insignificant difference ( $P > 0.05$ ) in serum sodium between group I and group II. Kumar, M. Hossain, Sood and their associates have found significant hyponatremia in neonates with seizure.<sup>2, 13, 9</sup> This significant decrease of sodium may be explained to be the result of water intoxication due to inappropriate secretion of antidiuretic hormone, which is secondary to asphyxia, intracranial hemorrhage meningitis, pneumonia & sepsis.

In the present study mean values of serum potassium yielded  $4.80 \pm 0.56$  and  $5.89 \pm 2.02$  in group I and group II respectively. Serum potassium increased significantly ( $P < 0.01$ ) in-group II (Cases) in comparison to group I (Control). The findings were comparable to studies carried out by Rao, Singhi .,; yuan ., a M. Hossain and their associates.<sup>12, 13, 14, 16</sup> The significant increase may be explained by increased potassium release as a result of tissue destruction due to trauma, hypothermia, bleeding, intravascular or extra vascular hemolysis, and asphyxia/ischaemia. Most of the condition was present in our study subjects. Sood and his associates in their study have found no change in potassium level<sup>9</sup>.

In the present study mean values of serum glucose of group I and group II yielded  $66.33 \pm 8.23$  and  $62.25 \pm 7.96$  respectively. The mean value in-group II (Cases) was lower than the mean value of group I (Control) but the difference was not significant. These findings were not comparable to studies carried out by Sood and his associates<sup>9</sup> and Kumar and his associate<sup>2</sup>. They included small for gestational age infants in their study whereas we did not include such infants in our group of cases. Hypoglycemia is most common in infants who are small for gestational age.

The presence of seizure does not constitute a diagnosis but it is a symptom of an underlying central nervous system disorder due to systemic and bio-chemical disturbance. Bio-chemical disturbances occur frequently in the neonatal seizure either as an underlying cause or associated abnormality. In their presence, it is difficult to control seizure and there is a risk of further brain damage. Early recognition and treatment of biochemical disturbances is essential for optimal management and satisfactory long-term outcome.

There are some limitations of our study as this study was done within the context of the facilities available to us. The number of patient in the present study was small due to shortage of time and refusal of parents to give consent for study. A study containing greater number of cases, with sufficient time and application of modern sophisticated technology are required to give a conclusive decision.

## Conclusion

Serum calcium in Group II (cases) is decreased significantly when compared with that of controls. Serum magnesium level in Group II (cases) is decreased significantly when compared with that of controls. Serum potassium level in Group II (cases) is increased significantly when compared with that of controls. There is no alteration in case of serum sodium and glucose level in neonates with seizure in this study. Most of the biochemical abnormalities in neonatal seizure are preventable and treatable conditions. But when left untreated control of seizure becomes difficult. Therefore, adequate antenatal care, safe delivery of babies, early detection and appropriate correction of biochemical abnormalities are suggested for reduction of neonatal morbidity and mortality from convulsive disorders. Therefore, it is very important that along with management of primary illness (like asphyxia, infection, prematurely) of a neonate, one needs to carefully and frequently monitor the biochemical status and make prompt and appropriate corrections to these abnormalities, which may be the cause of neonatal seizures or be their complications.

## References

1. Halsam RHA. Neonatal Seizures, In: Nelson Text Book of Paediatrics, 15<sup>th</sup> edn. Ed Behrman RE, Kliegman RM, Arvin AM. WB Saunders Company. Philadelphia. 1996; 1991-1996
2. Vasudevan C, Levene M. Epidemiology and aetiology of neonatal seizures. Seminars in Fetal and Neonatal Medicine 2013;18(4):185-191

3. Al-Zwaini EJ, Al-Ani MM, Mengal AH. The epidemiology of clinical neonatal seizures in Ramadi city. *Neurosciences Journal*. 2007;12(2):170-2
4. Gupte S. Neonatal seizures. In: *The short textbook of Pediatrics*. 6<sup>th</sup> ed. Ed. Gupte. Jaypee, New Delhi. 1989: 342
5. Rajput UC, Deshmukh LS. Predisposing risk factors for neonatal seizures in low birth weight babies: Case control study. *International Journal of Recent Trends in science and Technology*. 2014;10(3):508-14
6. Calciolari G, Periman JM, Volpe JJ. Seizures in the intensive care unit of the 1980s. Types, etiologies, timing. *Clin Pediatr*, 1988;27:119-123
7. Ghai OP. Newborn Infants, In: *Essential Pediatrics*, 4<sup>th</sup> ed, and Ed Ghai O P. Interprint. New Delhi. 1996;113-114
8. Kliegman RM. The Fetus and the Neonatal Infant, In: *Nelson Text Book of Paediatrics*, 15<sup>th</sup> edn. Behrman RE, Kliegman RM, Arvin AM. WB Saunders Company. Philadelphia. 1996, 469-512
9. Sood A, Grover N, Sharma R. Biochemical Abnormalities in Neonatal Seizures, 2003; 70:221
10. Amar. M. Taksande, Krishna Vilhekar, Manish Jain, Mahaveer Lakra, Wardha Clinico-Biochemical Profile of Neonatal Seizures, Department of Pediatrics, Mahatma Gandhi Institute of Medical Sciences, Sevagram,, Maharashtra; [www.pediatriconcall.com](http://www.pediatriconcall.com)
11. Kishore S. Agarwal, R. S. Beri and Jacob M. Puliyeel, Repeated Unifocal Seizure in Post Neonatal Infants with Hypocalcaemia, *Indian Pediatrics* 2000; 37
12. Hossain MM, Shirin M, Mamun MA, Chowdhury NA, Hasan MQ, Afroza S. Electrolyte abnormalities in neonates admitted in Intensive Care Unit. *Bangladesh J Child Health*. 2004;28(1):13-7
13. Kallem VR, Pandita A, Gupta G. Hypoglycemia: when to treat? *Clinical Medicine Insights: Pediatrics*. 2017 Dec 14;11:1179556517748913
14. Singhi S, Gulati S, Prasad SVSS. Frequency and significance of potassium disturbances in children. *Indian Pediatr* 1994;31:19-24
15. Yuan HC, Jeng MJ, Soong WJ, Chen SJ, Hwang BT. Hyperkalemia during the early postnatal days in premature infants. *Acta Paediatr Taiwan*. 2003; 44: 208-14