



TO STUDY THE PREVALENCE OF ELECTROLYTE IMBALANCE IN PATIENTS WITH SEIZURES

Kamlesh Kumar Sonkar

Professor Department of Medicine, MLN Medical College, Prayagraj.

Prince Kumar Singh*

Junior Resident Department of Medicine, MLN Medical College, Prayagraj.
*Corresponding Author

Anubha Srivastava

Professor Department of Medicine, MLN Medical College, Prayagraj.

ABSTRACT

Background: Seizure is defined as an episode of neurological dysfunction caused by abnormal neuronal activity that results in a sudden change in motor, behaviour and sensory perception¹.

Electrolytes seem to have a dominant role in the causation of seizures. Electrolyte homeostasis in the central nervous system (CNS) is a characteristic essential feature behind brain functioning. "A number of clinical studies have also shown a relationship between electrolyte imbalance and seizures.

OBJECTIVE: To Determine the Prevalence of electrolyte imbalance in patients with Seizures.

RESEARCH DESIGN AND METHODS: A cross sectional study was conducted at , MLN Medical College associated SRN Hospital, Prayagraj. A total 100 patients were enrolled in the study. Patients with 18 years of age or older presented with seizure as the presenting complaint were included. Patients presenting with cerebrovascular accident ,subarachnoid hemorrhage, tuberculoma cavernous sinus thrombosis febrile seizures hypoglycemia alcohol withdrawal uremic encephalopathy and patients refusing to participate in the study.

RESULT: Nearly two third (64%) patients had generalized tonic clonic seizures followed by focal seizures (27%) and status epilepticus (9%) respectively. Maximum electrolyte imbalance was seen for calcium (99%) followed by sodium (92%), potassium (63%) and magnesium (33%) respectively. A significant association of serum sodium status was observed with type of seizures with hyponatremia being more common in GTCS and hypernatremia being more common in status epilepticus.

Conclusion: In the present study, there was a high prevalence of hyponatremia (82%). Hyponatremia could be one of the most common factors leading to seizure activity. The findings of the present study shows that both in adults as well as in children show that electrolyte imbalance is a frequent observation in seizure activity, primarily cation deficiency is highly prevalent in seizure cases, however it is difficult to establish the role of a single electrolyte cation to be responsible for this activity.

KEYWORDS : Electrolyte, Seizure, Sodium, Potassium, Magnesium, Calcium.

INTRODUCTION:

Seizure (from Latin word *sacire*, "to take possession of") is a paroxysmal event due to abnormal excessive synchronous neuronal discharge activity in the brain. Seizure patients experience sudden alteration in consciousness, behaviour, memory or feelings.² There are a number of proposed pathophysiological mechanisms yet it is believed that a seizure takes place when there is distortion of the normal balance between excitation (E) and inhibition (I) in the brain³. Neuron membrane is permeable to electrolyte ions like calcium and sodium and permits them to pass from extracellular to intracellular region. Entry of these ions into intracellular environment affects the polarization status of neuron membrane resulting into release of excessive, irregular, and controlled electric charge. When this activity takes place at a large level in multiple neurons then it may result in seizures⁴. Regulation of ionic balance is a critical process involving a complex array of molecules for moving ions into and out of the brain and involving blood-brain barrier function as well as mechanism in the membranes of both neurons and glia. Alterations in ion gradients across cellular membranes can have direct and indirect effects on neuronal discharge and may facilitate epileptiform activities⁵. In clinical practice, hyponatremia and hypokalemia have frequently been seen in seizure patients while hypernatremia, hypercalcemia, hypermagnesemia and hyperkalemia have occasionally been seen in the seizures⁶.

MATERIAL AND METHODS

Study Design:

A cross sectional study was conducted at, MLN Medical College associated SRN Hospital, Prayagraj. A total 100 patients were enrolled in the study. Patients with 18 years of age or older presented with seizure as the presenting complaint were included. Patients presenting with

cerebrovascular accident, subarachnoid hemorrhage, tuberculoma cavernous sinus thrombosis febrile seizures hypoglycemia alcohol withdrawal uremic encephalopathy and patients refusing to participate in the study. Patients falling in eligibility criteria were included in the study after obtaining an informed consent. At enrolment, the demographic details (age and sex) of the patients were noted and diagnosis for type of seizure was made based on radiological (CT/MRI), clinical profile and specific investigations (EEG).

For serum electrolytes, the following range was considered as normal:

Serum sodium	135-145 mEq/L
Serum potassium	3.5-5 mEq/L
Serum Magnesium	≤1.6 mEq/L
Serum Calcium	2.2-2.5 mEq/L

RESULTS

A total of 100 seizure patients fulfilling the eligibility criteria were enrolled in the study

Table 1: Age and Sex Profile of patients enrolled in the study (n=100)

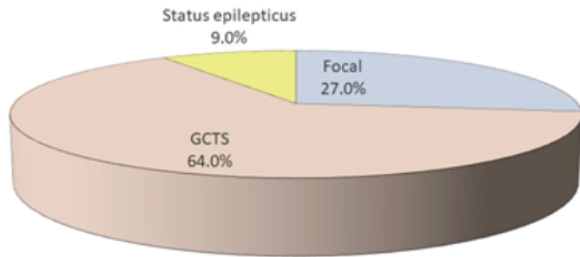
SN	Variable	No. / %
1.	Age	
	≤ 20 years	5
	21-30 years	9
	31-40 years	14
	41-50 years	13
	51-60 years	18
	61-70 years	23
	71-80 years	4
	81-90 years	12
	>90 years	2

	Mean age ± SD (Range) in years	54.22 ± 19.60 (18-92)
2.	Sex	
	Male	72
	Female	28

Age of patients ranged from 18 to 92 years. Majority of patients were in age range 41 to 70 years (54%). There were only 2 patients above 90 years of age. Mean age of patients was 54.22 ± 19.60 years. The study population was dominated by males (72%). The sex ratio (M:F) was 2.57.

Distribution of cases according to seizure type

Nearly two third (64%) patients had generalized tonic clonic seizures followed by focal seizures (27%) and status epilepticus (9%) respectively (Fig. 1).



Serum Electrolyte Profile

Serum sodium level ranged from 100.2 to 185.2 mEq/L with a mean of 119.97 ± 19.73 mEq/L. Serum potassium level ranged from 1.04 to 5.60 mEq/L with a mean of 3.53 ± 0.78 mEq/L. Serum magnesium level ranged from 0.40 to 2.10 mEq/L with a mean of 1.69 ± 0.32 and serum calcium level ranged from 0.80 to 5.20 mEq/L with a mean of 4.37 ± 0.80 mEq/L.

SN	Parameter	Mean	SD	Min	Max
1.	S. sodium (mEq/L)	119.97	19.73	100.2	185.2
2.	S. Potassium (mEq/L)	3.53	0.78	1.04	5.60
3.	S. magnesium (mEq/L)	1.69	0.32	0.40	2.10
4.	S. calcium (mEq/L)	4.37	0.80	0.80	5.20

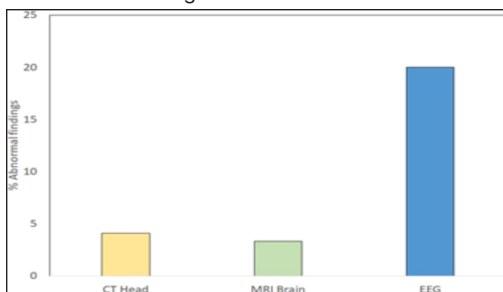
Distribution of cases according to Serum Electrolyte Status

There was a wide derangement of electrolytes. Maximum derangement was seen for calcium (99%) followed by sodium (92%), potassium (63%) and magnesium (33%) respectively (Table 5; Fig. 5). Hyponatremia, normonatremia and hypematremia were seen in 82%, 8% and 10% cases respectively. Hypokalemia, normokalemia and hyperkalemia were seen in 54%, 37% and 9% cases respectively. Hypomagnesemia, normomagnesemia and hypermagnesemia were seen in 33%, 67% and 0% cases respectively. Hypocalcemia, normocalcemia and hypercalcemia were seen in 5%, 1% and 94% cases respectively.

SN	Serum Electrolyte (Normal range mEq)	Below normal range	Normal range	Above normal range
1.	Sodium (135-145)	82	8	10
2.	Potassium (3.5-5)	54	37	9
3.	Magnesium (<1.6)	33	67	0
4.	Calcium (2.2-2.5)	5	1	94

Specific Investigation findings

CT, MRI and EEG investigations were carried out in 98, 61 and 45 patients respectively. Abnormal findings were seen in 4.1%, 3.3% and 20% of investigated cases



(Fig. 2).

Table 2: Final Outcome

SN	Variable	No. / %
1.	Hospital stay	
	<5 days	76
	>5 days	24
	Mean duration of hospital stay ± SD (Range) in days	4.46 ± 1.95 (1-10)
2.	Outcome	
	Discharge after recovery	85
	Referred	15

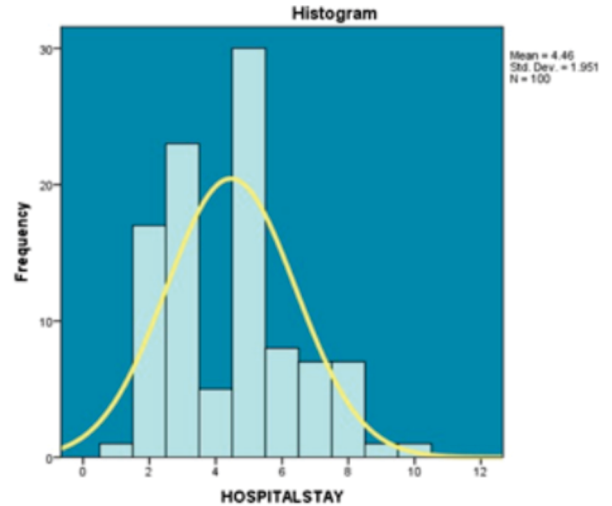


Fig. 3: histogram Showing Dispersion Of Hospital Stay Duration

Final outcome

Duration of hospital stay ranged from 1 to 10 days with a mean of 4.46 days. A total of 76 patients had hospital stay ≤5 days and remaining 24 had hospital stay >5 days. A total of 85 patients were discharged after recovery while 15 were referred to other facility. There was no in-hospital mortality.

DISCUSSION

Electrolytes can be both cations as well as anions and have a diversified spectrum. In past, derangement of some cations like sodium^{7,8,9}, potassium^{9,10,11}, iron¹², calcium^{9,11,12,13} magnesium^{9,11,12,14}, zinc^{9,15} and phosphorous^{11,13} have been explored for their relationship with seizure, however, there are no uniform trends across different studies despite some studies endorsing this relationship^{7,8,9,13} while at the same time there are studies that do not find an association of electrolyte imbalance with seizures¹². Some other studies found a selective association of some particular types of seizures with electrolyte imbalance¹⁶. In the present study, nearly two third (64%) patients had generalized tonic clonic seizures followed by focal seizures (27%) and status epilepticus (9%) respectively. Among studies in adults, Mohanta *et al.*¹⁷ too reported a dominance of generalized tonic-clonic seizures (73%) as also observed in the present study. In their study, the other seizure type was focal (30%) and there was no case of status epilepticus. Dhadke *et al.*¹⁸ in another study among adults also found dominance of generalized seizures (76%) over focal seizures (24%), however, they did not describe the proportion of status epilepticus patients separately.

In the present study, mean serum sodium, potassium, magnesium and calcium levels were 119.97 ± 19.73, 3.53 ± 0.78, 1.69 ± 0.32 and 4.37 ± 0.80 mEq/L respectively. Among all these, mean values of serum sodium were below the normal defined range (135-145 mEq/L), for serum potassium the values were just close to the lower value of normal range (3.5-5 mEq/L). For magnesium, the mean value was just close to normal range (<1.6 mEq/L) whereas mean calcium levels were above the defined normal range (2.2-2.5

mEq/L). Correspondingly we found majority of cases having serum sodium levels below the normal range (82%), potassium levels below the normal range (54%), magnesium levels within normal range (67%) and calcium levels above normal range (94%). As far as electrolyte imbalance was concerned, it was most dominant for serum calcium and serum sodium where only 1% and 8% patients respectively had levels within normal range. The electrolyte imbalance was least pronounced for magnesium where 67% cases had values within normal range. As far as sodium and calcium levels are concerned, both of them have been reported to be instrumental in initiating the seizure activity^{19,20}. Compared to the present study, Namakian *et al.*⁹ who also assessed the four electrolytes (serum sodium, potassium, magnesium and calcium) reported the mean values in cases to be 136.2 ± 3.3 , 4.38 ± 0.41 , 8.79 ± 0.47 and 1.9 ± 0.32 respectively in children with febrile seizures. Compared to the present study, seizure patients in their study had serum sodium, potassium and magnesium levels much higher while serum calcium levels were much lower. It must be however taken into consideration that their study was carried out in children and included febrile seizure patients. In the present study, though we found prevalence of hypomagnesemia to be 37%, however, only 5 patients with hypocalcemia and hypercalcemia was the dominant issue (94%). Association of low magnesium levels with seizure activity in adults was also established by Abdulalahi *et al.*¹¹ in their study. In the present study, there was a high prevalence of hyponatremia (82%). Hyponatremia could be one of the most common factors leading to seizure activity as also shown by Halawa *et al.*⁸ who found that with decreasing serum sodium levels the odds of seizure increase substantially. The high prevalence of hyponatremia in the present study also endorsed this relationship. The findings of the present study and its comparison with previous studies, both in adults as well as in children show that electrolyte imbalance is a frequent observation in seizure activity, primarily cation deficiency is highly prevalent in seizure cases, however it is difficult to establish the role of a single electrolyte cation to be responsible for this activity. The present study had excluded a number of underlying conditions which were otherwise not excluded in the previous studies. Moreover, most of the contemporary literature studying the relationship between electrolyte imbalance and seizure is coming from childhood febrile seizure cases. The present study, thus within the defined limits of its study population showed a high prevalence of hyponatremia and high prevalence of hypercalcemia as the distinct electrolyte imbalances in adult non-febrile seizure patients without any chronic and acute underlying confounding condition. In the present study, we found an association of serum sodium levels with type of seizures with hyponatremia being more common in GTCS and hypernatremia being more common in status epilepticus.

CONCLUSIONS

The present study assessed association between seizure and electrolyte imbalance. For this purpose a total of 100 seizure patients (age range 18-92 years; Mean age 54.22 ± 19.60 years; 72% males) were enrolled in the study and were evaluated clinically and biochemically followed by serum electrolyte (Sodium, potassium, magnesium and calcium). Nearly two third (64%) patients had generalized tonic clonic seizures followed by focal seizures (27%) and status epilepticus (9%) respectively. Mean serum sodium, potassium, magnesium and calcium levels were 119.97 ± 19.73 ; 3.53 ± 0.78 , 1.69 ± 0.32 and 4.37 ± 0.80 mEq/L respectively. Maximum electrolyte imbalance was seen for calcium (99%) followed by sodium (92%), potassium (63%) and magnesium (33%) respectively. Hyponatremia, normonatremia and hypernatremia were seen in 82%, 8% and 10% cases respectively. Hypokalemia, normokalemia and hyperkalemia were seen in 54%, 37% and 9% cases respectively. Hypomagnesemia, normomagnesemia and hypermagnesemia were seen in 33%, 67% and 0% cases respectively. Hypocalcemia,

normocalcemia and hypercalcemia were seen in 5%, 1% and 94% cases respectively. A significant association of serum sodium status was observed with type of seizures with hyponatremia being more common in GTCS and hypernatremia being more common in status epilepticus. None of the serum electrolytes studied showed any significant association with final outcome.

REFERENCES:

- 1 Stafstrom CE, Carmant L. Seizures and epilepsy: an overview for neuroscientists. *Cold Spring Harb Perspect Med.* 2015;5(6):a022426. Link
- 2 Huff JS, Murr N. Seizure. [Updated 2021 Jul 25]. In: Stat Pearls [Internet]. Treasure Island (FL): Stat Pearls Publishing; 2021 Jan-. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK430765/>
- 3 Stafstrom CE. Pathophysiological mechanisms of seizures and epilepsy: A primer. In *Epilepsy: Mechanisms, models, and translational perspectives* (ed. Rho JM, Sankar R, Stafstrom CE). 2010. CRC, Boca Raton, FL, pp. 3–19.
- 4 Haurer Stephen L.In: Harrison's Neurology In clinical Medicine. 2013, USA: Mc Graw Hill Education.
- 5 Schwartzkroin PA, Baraban SC, Hochman DW. Osmolarity, ion flux, and changes in brain excitability. *Epilepsy Research* 1998; 32:275–285.
- 6 Castilla-Guerra L, del Carmen Fernández-Moreno M, López-Chozas JM, Fernández-Bolaños R. Electrolytes disturbances and seizures. *Epilepsia.* 2006 Dec;47(12):1990-8. Link
- 7 Nadkarni J, Binaykiya I, Sharma U, Dwivedi R. Role of serum sodium levels in prediction of seizure recurrence within the same febrile illness. *Neurology Asia* 2011; 16(3): 195–197. Link
- 8 Halawa I, Andersson T, Tomson T. Hyponatremia and risk of seizures: a retrospective cross-sectional study. *Epilepsia.* 2011 Feb;52(2):410-3. Link
- 9 Usha Kiran CB, Suresh R. Reduced serum calcium is a risk factor for febrile seizures. *Int J Contemp Pediatr* 2017;4:1506-8. Link
- 10 Charan J, Biswas T. How to calculate sample size for different study designs in medical research? *Indian J Psychol Med.* 2013 Apr;35(2):121-6.
- 11 Kwak BO, Kim K, Kim SN, Lee R. Relationship between iron deficiency anemia and febrile seizures in children: A systematic review and metaanalysis. *Seizure.* 2017 Nov;52:27-34. Link
- 12 Rama Krishna C, Basha SJ, Venkateswara Rao B, Preethi B. Serum Magnesium Levels in Seizure Disorders. *Journal of Evolution of Medical and Dental Sciences* 2014; 3(35): 9313-9319. Link
- 13 Namakian K, Zardast M, Sharifzadeh G, Bidar T, Zargarian S. Serum Trace Elements in Febrile Seizure: A Case-Control Study. *Iran J Child Neurol.* 2016;10(3):57-60. Link
- 14 Mohanta SK, Naik M, Murmu M. Study of Serum Magnesium and Calcium Levels in Patients with new onset Seizures. *JMSCR* 2019; 7(3): 1320-1326. Link
- 15 Chen BB, Prasad C, Kobrzynski M, Campbell C, Filler G. Seizures Related to Hypomagnesemia: A Case Series and Review of the Literature. *Child Neurol Open.* 2016;3:2329048X16674834. Link
- 16 Abdullahi I, Watila M M, Shahi N, Nyandaiti Y W, Bwala S A. Serum magnesium in adult patients with idiopathic and symptomatic epilepsy in Maiduguri, Northeast Nigeria. *Niger J Clin Pract* 2019;22:186-93. Link
- 17 Sambyal V, Chandail VS. A study of clinical profile of seizure disorder at tertiary care centre a retrospective cross sectional study. *International Journal of Current Research* 2019; 11(5): 2541-2543. Link
- 18 Dhadke VN, Dhadke SV, Dawar A. Clinical profile of seizure disorder in hospitalized patients. *Int J Adv Med* 2016;3:275-81. Link
- 19 Stafstrom CE. Persistent sodium current and its role in epilepsy. *Epilepsy Curr.* 2007;7(1):15-22. Link
- 20 Han P, Trinidad BJ, Shi J. Hypocalcemia-induced seizure: demystifying the calcium paradox. *ASN Neuro.* 2015;7(2):1759091415578050. Link