Estimating the prevalence of hypocalcemia in adults presenting with new-onset seizures: A cross-sectional study

By Sharan Bose

WORD COUNT 2299
TIME SUBMITTED 15-MAY-2024 05:08PM
PAPER ID 108989794

Word Count – Words: 2,295

Research article

Estimating the prevalence of hypocalcemia in adults presenting with new-onset seizures: A cross-sectional study

---

Sharan Bose, K.V. Rajalakshmi, Anantha Kumar P.K, Bhuvaneshwar, Jibin Simon

Department of General Medicine, Saveetha Medical College and Hospital, Saveetha Institute of Medical and Technical Sciences, Thandalam, Chennai, India

Corresponding author:
Sharan Bose
E-mail: sharanbose7@gmail.com

ABSTRACT

Background: Approximately 8% to 10% of the population will experience a seizure during their lifetime. Only about 2% to 3% of patients go on to develop epilepsy**.** Common metabolic causes include hypoglycemia, hyperglycemia, hyponatremia, hypocalcemia, hypomagnesemia, etc. Hypocalcemia in particular is often implicated in neonates and younger children. The present study was aimed at estimating the prevalence of hypocalcemia in adults (>18 years of age) presenting with new onset seizures.

Material and Methods: Our study was a cross-sectional, prospective, observational study, conducted in patients aged more than 18 years of age of either sex who presented with at least 1 episode of acute (< 24 hrs) new onset seizures. Venous blood was collected in a red top plastic tube, containing no anticoagulants and used for laboratory testing.

Results: During the study period, 72 patients with new-onset seizures were considered for the present study. The mean age of the study population was 44.73 ± 12.45 years. The mean serum calcium level was 8.8 ± 0.53 mg / dL. Serum calcium level less than 8.5 mg/dL was noted in 32 cases (44.44 %). A level in the normal range (8.5 - 10 mg/dl) was noted in 40 patients (55.56 %). A serum albumin level of less than 3 gm % was noted in 7 patients (9.72 %). The mean corrected serum calcium level was 8.23 ± 0.71 mg / dL. Among 72 patients, a corrected serum calcium level of less than 8.5 mg/dL was noted in 31 cases. Thus, the prevalence of hypocalcemia in adults presenting with new-onset seizures was 43.05 %. There was no significant difference noted for age & gender among hypocalcaemic & normocalcaemic cases ($p > 0.05$).

Conclusion: In patients presenting with new onset seizures, the prevalence of hypocalcemia was found to be 43%. Further studies are required to prove definite causality. However, we recommend checking Sr. Calcium levels, along with the other electrolytes for all patients presenting with new onset seizures and correcting them as required.

Keywords: new onset seizures, hypocalcemia, serum calcium levels, electrolyte disturbances.

INTRODUCTION

About 8% to 10% of people will experience seizures at some point in their lives, but only 2% to 3% of those people will go on to develop epilepsy [1]. A new-onset seizure may indicate the early stages of epilepsy, brain infections, stroke, metabolic problems, brain tumors, systemic disorders, or any combination of these conditions, requiring careful assessment and treatment [2].

Seizures can have a variety of causes, and the type of seizure and whether it is induced or not are important considerations. Seizures are largely caused by metabolic disorders, which include hypo-, hyperglycemia, hyponatremia, hypocalcemia, and hypomagnesemia [3,4]. Interestingly, despite its frequent association with newborns and younger children, hypocalcemia-induced seizures are thought to be underreported among adults having new-onset seizures, despite its potential to heighten neuromuscular irritability and precipitate neurological manifestations like tetany, delirium, and seizures.

Specifically, acute hypocalcemia increases the likelihood of neuromuscular irritability and seizure activity; possible early symptoms include generalized tonic-clonic seizures (GTCS), absence, and focal seizures [5]. Owing to the intricacy of the etiology of seizures, a thorough assessment of patients having their first seizure is necessary in order to determine the type of seizure, pinpoint contributing factors, and clarify underlying, potentially curable etiologies. This will enable the implementation of effective treatment and recurrence prevention strategies.

In order to fill this gap in the literature, our current study aims to estimate the prevalence of hypocalcemia in persons over the age of 18 who are presenting with new-onset seizures.

MATERIAL AND METHODS

Our study was a cross-sectional, prospective, observational study, conducted in a tertiary care center in South India. The study duration was of 6 months (March 2023 to September 2023). Study approval was obtained from the institutional ethical committee.

Inclusion criteria:

- All patients aged more than 18 years of age of either sex who presented with at least 1 episode of acute (< 24 hrs) clinically defined seizure (the type of seizure was established according to the ILAE 2017 classification of seizures.), willing to participate in the study

Exclusion criteria:

- Patients having a previous history of seizures/epilepsy.
- Patients on calcium or Vitamin D supplementation.
- Patients with brain imaging showing major abnormalities that may be the cause for the seizures, eg. Space occupying lesions, encephalitis, evidence of previous strokes, structural abnormalities, hydrocephalus, vascular abnormalities etc.
- Patients with serum sodium level >150 mg/dl, or <130 mg/dl.
- Patients with serum magnesium level < 1.6 mg/dl.
- Patients with serum glucose > 250 mg/dl, or <70 mg/dl.

The study was explained to the patients in their local language & written consent was taken for participation in the study. They were interviewed as per the proforma and a complete clinical examination was done. Cases of new-onset seizures were diagnosed with clinical history, examination, laboratory and radiological studies.

Routine laboratory investigations were done in all cases at admission including a complete hemogram, ESR, serum electrolytes (sodium, potassium, magnesium, and calcium), liver function tests, renal function tests, random blood sugar, and serum albumin. Brain imaging in the form of a CT or MRI scan was done in all cases. Venous blood was collected in a red top plastic tube, containing no anticoagulants and used for laboratory testing.

Data was collected and compiled using the Microsoft Excel software and analyzed using the SPSS 23.0 software. Frequency, percentage, means and standard deviations (SD) were calculated for

the continuous variables, while ratios and proportions were calculated for the categorical variables. Differences in proportions between qualitative variables were tested using the chi-square test or Fisher's exact test as applicable. A P value of less than 0.05 was considered statistically significant.

RESULTS

During the study period, 72 patients with new-onset seizures were considered. The mean age of the study population was 44.73 ± 12.45 years. The most common age groups were 21-30 years (26.39 %) followed by 51-60 years (25 %). Generalized tonic-clonic seizures were the most common type of seizures encountered (75 %).

Table 1- General characteristics

Characteristic	No. of patients	Percentage
Age groups (in years)		
19-20	7	9.72
21-30	19	26.39
31-40	10	13.89
41-50	10	13.89
51-60	18	25
61-70	5	6.94
>70	3	4.17
Mean age (mean ± SD)	44.73 ± 12.45	
Gender		
Male	45	62.5
Female	27	37.5
Type of seizure		
GTCS (Generalised tonic-clonic seizure)	54	75
Focal	9	12.5
Unclassified	8	11.11
ABSENCE	1	1.39

The mean serum calcium level was 8.13 ± 0.53 mg/dL. A serum calcium level of less than 8.5 mg/dL was noted in 32 cases (44.44 %). A level in the normal range (8.5 - 10 mg/dl) was noted in 40 patients (55.56 %).

Table 2- Serum calcium levels

	No. of patients	Percentage
<7	1	1.39
7-7.5	4	5.56
7.6-8	7	9.72
8.1-8.5	21	29.17
8.6-9	23	31.94
9.1-9.5	12	16.67
>9.5	4	5.56

A serum albumin level of less than 3 gm % was noted in 7 patients (9.72 %), while the majority had a serum albumin level of 3.1-4 gm % (54.17 %).

Table 3- Serum albumin levels

	No. of patients	Percentage
<2	1	1.39
2.1-3	6	8.33
3.1-4	39	54.17
4.1-5	24	33.33
>5	2	2.78

The mean corrected serum calcium level was 8.23 ± 0.71 mg / dL. The total number of patients with hypocalcemia (ie; corrected serum calcium levels less than 8.5 mg/dl) were 31 (43.05%) with a p value of 0.0001.

Table 4- Corrected Serum calcium levels

	No. of patients	Percentage
<7.5	3	4.17
7.5-8	10	13.88
8.1-8.5	18	25
8.6-9	24	32.33
9.1-9.5	11	15.28
>9.5	6	8.33

There was no significant difference noted for age & gender among hypocalcaemic and normocalcaemic cases ($p > 0.05$).

Table 5- Comparison of hypocalcaemic & normocalcaemic cases

Characteristic	Hypocalcaemic cases	Normocalcaemic cases	P value
Mean age (mean ± SD)	48.44 ± 10.84	43.26 ± 11.76	0.057
Gender			0.199
Male	27 (69.2 %)	18 (54.5%)	
Female	12 (31.8%)	15 (46.5%)	

DISCUSSION

Total blood calcium concentrations normally range from 8.5 to 10.3 mg/dL, which is corresponding to 2.2 to 2.6 mmol/L and 4.4 to 5.2 mEq/L [6,7]. About 50% of serum calcium is ionized, while the remainder is bound to albumin or other ions in the blood. The content of albumin is the most important factor that can change the ratio of bound calcium to ionized calcium. Serum albumin levels might drop as a result of certain medical disorders. As a result, serum calcium concentrations are "corrected" to 40 g/l, or 4 mg/dL, of reference albumin concentration. The calcium is changed by 0.02 mmol/L for each 1 g/l (or 1 mg/dL) of albumin that is above or below this threshold [6, 7].
A frequent biochemical anomaly, hypocalcemia can range in severity from mild cases with no symptoms to severe ones that could be fatal [8]. While the remaining free ionized calcium in the serum is physiologically active, almost half of the total calcium content is bound to proteins [9]. To diagnose hypercalcemia or hypocalcemia, serum calcium values must be adjusted for albumin levels [8].

Hypocalcemia is frequently caused by vitamin D deficiency, but in patients who have had thyroidectomies, severe hypocalcemia is typically linked to iatrogenic hypoparathyroidism [8,9,10]. Additional reasons include end-stage renal or liver illness, autoimmune hypoparathyroidism, heavy

metal invasion of the parathyroid gland, hypo- or hypermagnesemia, Hungry bone syndrome, and Fanconi syndrome [11]. Antiepileptics, aminoglycosides, cisplatin, bisphosphonates, and diuretics [12] are a few medications that might cause hypocalcemia.

Because of the increased excitability of the central nervous system, hypocalcemia can cause a variety of neurological symptoms such as delirium, seizures, and tetany. Chvostek's sign, which appears as hyperexcitability in the facial muscle nerve endings, is a sensitive clinical indicator of hypocalcemia [13]. Patients with renal insufficiency or underlying endocrinological disorders with overall poor calcium homeostasis are more prone to experience hypocalcemia-induced seizures [14].

The difference between the blood calcium levels of epileptic seizure cases (6.28 ± 2.86 mg/dL) and healthy control (9.49 ± 0.80 mg/dL) was shown to be statistically significant in a study by Sharma S et al. [15]. The study recommended routine calcium screening for individuals experiencing epileptic seizures [15]. According to Kachapur C et al. [16], 64.9% of patients with breakthrough seizures who had epileptic seizures had a total serum calcium level of less than 8.5 mg/dL. The mean serum calcium in these patients was 8.36 ± 0.45 mg/dL. Increased incidence of breakthrough seizure episodes was also linked to lower serum calcium levels [16].

In our study, 43% of patients with newly onset seizures had hypocalcemia. Antiepileptic medication should not be started until all metabolic diseases that can be treated have been ruled out. Many patients will be released from unnecessary burden of polytherapy. The current study did not find any possible dangers. The study's limitations were the potential for human error in sample collection and biochemical testing, as well as the lack of ionized calcium testing.

CONCLUSION

In our investigation, we found that 43% of patients presenting with new onset seizures had hypocalcemia. Seizures serve as significant clinical manifestations of electrolyte disturbances. Therefore, assessing electrolyte levels, especially Sr. Calcium levels should be integrated into the initial diagnostic evaluation of adult patients experiencing new onset seizures. This proactive approach can aid in identifying and addressing potentially treatable metabolic imbalances, thereby optimizing patient care and management strategies, and preventing long term burdensome antiepileptic therapy.

Conflict of Interest: None to declare
Source of funding: Nil

REFERENCES

1. Gavvala JR, Schuele SU. New-Onset Seizure in Adults and Adolescents: A Review. *JAMA*. 2016;316(24):2657-2668. doi:10.1001/jama.2016.18625
2. Shorvon SD, Andermann F, Guerrini R. The causes of epilepsy. Cambridge University Press, Cambridge. Epilepsia 2011;52:1033–44.
3. Mahmoud MH, Awad, EM, Mohamed AK, Shafik MA. Etiological profile of new-onset seizures among adult Egyptians. Egypt J Neurol Psychiatry Neurosurg 2021;57:95.
4. Bhatia MS, Attri R, New onset seizures in critically ill patients admitted in intensive care units: A preliminary study. J Med College Chandigarh 2018;8:10—3.
5. Han P, Trinidad BJ, Shi J. Hypocalcemia-induced seizure: demystifying the calcium paradox. ASN Neuro 2015;7(2):1759091415578050.
6. Bushinsky DA, Monk RD. Electrolyte quintet: calcium. Lancet 1998;352:306-11.
7. Cooper MS, Gittoes NJ. Diagnosis and management of hypocalcaemia. BMJ. 2008 Jun 7;336(7656):1298-302.
8. Cooper MS, Gittoes NJ. Diagnosis and management of hypocalcaemia. BMJ 2008;336(7656):1298-302.
9. Murphy E, Williams GR. Hypocalcaemia. Medicine 2009;37(9):465-8.

10. Prendiville S, Burman KD, Wartofsky L, Ringel M, Sessions R. Evaluation and treatment of post-thyroidectomy hypocalcemia. Endocrinologist 1998;8(1):34.
11. Fong J, Khan A. Hypocalcemia: updates in diagnosis and management for primary care. Can Fam Physician 2012;58(2):158–162.
12. Liamis G, Milionis HJ, Elisaf M. A review of drug-induced hypocalcemia. J Bone Miner Metab 2009;27(6):635–642.
13. Milman, S., & Epstein, E. J. (2010). Proton pump inhibitor-induced hypocalcemic seizure in a patient with hypoparathyroidism. Endocrine Practice, 17, 104–107.
14. Morton, A. R., Garland, J. S., & Holden, R. M. (2010). Is the calcium correct? Measuring serum calcium in dialysis patients. Seminars in Dialysis, 23, 283–289.
15. Sharma S, Fiza B, Tiwari SK, et al. Evaluation of Serum Calcium Levels in Patients with Epileptic Seizure. J Mahatma Gandhi Univ Med Sci Tech 2020;5(2):35–37.
16. Kachapur C, Kallimani SN, Gayathri BH, et al. A study of serum calcium and magnesium levels in idiopathic epilepsy patients of Hubli, Karnataka, India. J Evid Based Med Healthc 2021;8(25):2187-2191.
17. Al-Janabi JM, Marbut MM, Ahmed BS, et al. Determination of calcium & magnesium in the serum of epileptic patients. Tikrit Med J 2005;11(2):41-43.
18. Prasad DKV, Shaheen U, Satyanarayana U, et al. Association of serum trace elements and minerals with genetic generalized epilepsy and idiopathic intractable epilepsy. Neurochem Res 2014;39(12):2370-2376.