

A Study of Serum Calcium and Magnesium Levels in Idiopathic Epilepsy Patients of Hubli, Karnataka, India

Chandrashekar Kachapur¹, Seetaram N. Kallimani², Gayathri B.H.³, Ishwar S. Hasabi⁴, Zahura M. Devarhoru⁵

^{1, 2, 3, 4, 5} Department of General Medicine, Karnataka Institute of Medical Sciences, Hubli, Karnataka, India.

ABSTRACT

BACKGROUND

Magnesium is a potential modulator of seizure activity because of its ability to antagonize the excitatory calcium influx through N-methyl-D-aspartate (NMDA) receptor which is thought to play a role in many human forms of epilepsy. When the extracellular concentration of calcium ion falls below normal, the nervous system becomes more excitable, allowing easy initiation of action potentials. Consequently, hypocalcaemia causes seizures because of its action of increasing excitability in the brain. We wanted to estimate the serum concentration of calcium and magnesium in idiopathic epilepsy patients and its co-relation.

METHODS

94 cases of idiopathic epilepsy with breakthrough seizures admitted to KIMS Hospital, Hubli, meeting the inclusion criteria were considered for the study which was for 2-years' time period. It's a single centred, time bound and cross sectional study.

RESULTS

Mean serum calcium was low 8.36 ± 0.45 mg / dL and mean serum magnesium was 1.79 ± 0.28 mg / dL. 64.9 % had total serum calcium less than 8.5 mg / dL and 44.7 % had serum magnesium of < 1.8 mg / dL. 35.1 % had both low calcium and magnesium. There was significant difference in mean serum calcium with respect to number of episodes. There was no significant difference in mean serum magnesium with respect to number of episodes.

CONCLUSIONS

Serum calcium and magnesium levels which play a role in seizure initiation should be measured in all idiopathic epilepsy patients with breakthrough seizures as a seizure trigger. Considering the role of calcium and magnesium in the pathophysiology of seizures and by evaluating the results from the present study, breakthrough seizure could be provoked by hypocalcaemia and hypomagnesemia. Hence they may be used for the treatment of intractable seizures.

KEYWORDS

Calcium, Magnesium, Idiopathic Epilepsy

Corresponding Author:

*Dr. Zahura M. Devarhoru,
Hashmi Manzil, 1st Cross,
Vinayak Nagar, Navalur,
Dharwad - 580009, Karnataka, India.
E-mail: zahuramz@gmail.com*

DOI: 10.18410/jebmh/2021/409

How to Cite This Article:

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. DOI: 10.18410/jebmh/2021/409

Submission 02-02-2021,

Peer Review 12-02-2021,

Acceptance 04-05-2021,

Published 21-06-2021.

Copyright © 2021 Chandrashekar Kachapur et al. This is an open access article distributed under Creative Commons Attribution License [Attribution 4.0 International (CC BY 4.0)]

BACKGROUND

Epilepsy is one of the most serious neurological conditions and has an impact not only on the affected individual but also on the family and, indirectly, on the community.¹ Health related quality of life scores are significantly lower in patients with epilepsy than in the general public and seizure frequency is a good predictor of quality of life. Cognitive difficulties limit effective social and occupational functioning in these patients.² The psychiatric problems associated with epilepsy include depression, anxiety, and psychosis.³

The clinical presentations as well as the causes for seizures vary in different age groups and in different regions. Some of the most important causes of focal seizures are post stroke epilepsy, calcified granuloma, neurocysticercosis, tuberculoma, idiopathic, brain tumour, brain abscess and meningitis in that order and vascular, metabolic, infection, cryptogenic, traumatic etc. for generalized seizures.³ Seizures beginning in adult life are likely due to an identifiable cause as compared to those beginning in childhood which is more likely to be idiopathic.⁴ The most common cause of epilepsy is now believed to be genetic in origin. Even seizures in known epileptic patients can only be explained by subtherapeutic antiepileptic drug levels 60 % of the time.⁵ Magnesium is a potential modulator of seizure activity because of its ability to antagonize the excitatory calcium influx through NMDA receptor which is thought to play a role in many human forms of epilepsy.^{6,7} The activation of NMDA receptor by excitatory amino acids results in calcium influx recognised for its pro-epileptogenic effects.^{8,9} The inhibition of NMDA glutamate receptors and the increased production of vasodilator prostaglandins in the brain is the anti-convulsant action of magnesium.¹⁰ Magnesium serves to stabilize neuronal membranes and the lack of it explains the tendency to have seizures.¹¹

When the extracellular concentration of calcium ion falls below normal, the nervous system becomes more excitable, because this causes neuronal membrane permeability to sodium ions allowing easy initiation of action potentials. At plasma calcium ion concentration about 50 % below normal, the peripheral nerve fibres become so excitable that they begin to discharge spontaneously, initiating train of nerve impulses that passes to the peripheral skeletal muscles to elicit tetanic muscle contraction. Consequently, hypocalcaemia causes tetany and seizures because of its action of increasing excitability in the brain.¹⁰ Hence the present study was taken up to estimate the serum concentration of calcium and magnesium in idiopathic epilepsy patients and its co-relation.

METHODS

This is a cross sectional study conducted in the Department of General Medicine, Karnataka Institute of Medical Sciences (KIMS), a tertiary care hospital situated in Hubli from November 2017 to October 2019. The study was conducted among the patients with idiopathic epilepsy with breakthrough seizures after obtaining ethical clearance from the institutional ethics committee [Ref no.

KIMS/PGS/SYN/447/2017-18] and informed consent from the participants.

Inclusion Criteria

- All patients with idiopathic epilepsy with breakthrough seizures
- Age between 18 and 60 years

Exclusion Criteria

- Space occupying lesions in brain
- Scar epilepsy
- Cerebrovascular accidents
- Head injury
- Chronic kidney disease
- Diuretic therapy
- Bone disorder
- Carcinoma of lung, breast and kidney
- Neuroinfection.
- Malabsorption disorders
- Patients receiving calcium & magnesium supplements

The following investigations were done and analysed. Serum calcium and magnesium were measured using spectrophotometric method with arsenazo reagent and xylidyl blue reagent respectively.

- Complete haemogram
- Random blood sugar
- Renal function test
- Liver function test
- Serum electrolytes – Sodium, Potassium, Calcium, Magnesium
- Electroencephalogram
- Computed Tomography of Brain-Plain.
- Computed Tomography of Brain-Contrast (if required)
- Cerebrospinal fluid analysis (if necessary)
- Magnetic Resonance Imaging of Brain (if required)

Normal Ranges

Serum calcium: 8.5 to 10.5 mg / dL

Serum magnesium: 1.8 to 2.4 mg / dl

Statistical Analysis

Data was entered into Microsoft excel data sheet and was analysed using SPSS 22 version software (IBM SPSS statistics, Somers NY, USA). Categorical data was represented in the form of Frequencies and proportions. chi-square test was used as test of significance for qualitative data. Continuous data was represented as Mean and SD. Independent t test was used as test of significance to identify the mean difference between two quantitative variables. ANOVA (Analysis of Variance) was the test of significance to identify the mean difference between more than two groups for quantitative data. Graphical representation of data: MS Excel and MS word was used to obtain various types of graphs such as bar diagram and Scatter plots. P value (Probability that the result is true) of

< 0.05 was considered as statistically significant after assuming all the rules of statistical tests.

RESULTS

In the study mean age of subjects was 34.43 ± 13.56 years. 64 subjects were males and 30 of them were females. In the study 97.9 % were generalized seizures and 2.1 % were focal seizures. Among females mean calcium was 8.393 ± 0.416 mg / dL and among males was 8.337 ± 0.472 mg / dL. Among females mean Magnesium was 1.78 ± .26 mg / dL and among males was 1.80 ±.29 mg / dL.

There was significant difference in Mean serum calcium with respect to number of episodes. Mean serum calcium was high among those with one episode (8.57 ± .26 mg / dL) and low among those with 4 episodes of epilepsy (7.58 ± .39 mg / dL), suggesting that there was decrease in mean serum calcium with respect to number of episodes.

There was no significant difference in mean magnesium with respect to number of episodes. Mean calcium among those with focal seizures was 8.32 ± 0.56 and among those with generalized seizures was 8.36 ± 0.43. There was no significant difference in mean calcium between types of seizures. In the study 64.9 % had serum calcium < 8.5 mg / dL and 35.1 % had calcium levels of 8.5 to 10.5 mg / dL.

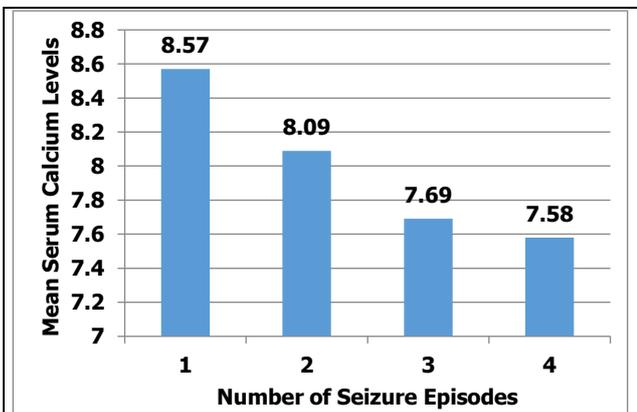


Figure 1. Mean Serum Calcium Levels with Respect to Number of Episodes

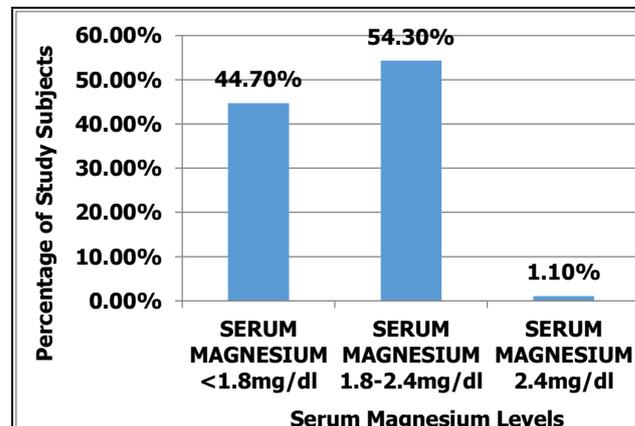


Figure 3. Distribution of Serum Magnesium in the Study Subjects

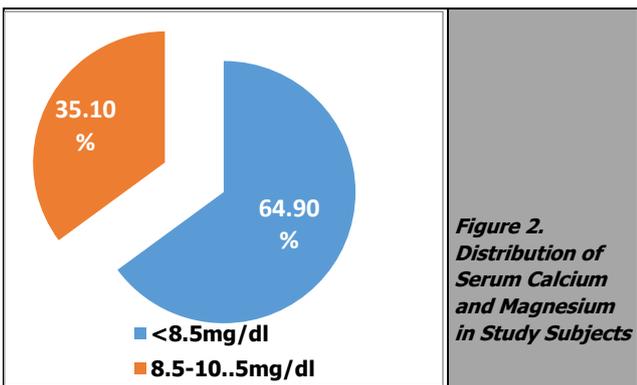


Figure 2. Distribution of Serum Calcium and Magnesium in Study Subjects

In the study 44.7 % had serum magnesium of < 1.8 mg / dL, 54.3 % had magnesium of 1.8 to 2.4 mg / dL and 1.1 % had magnesium of > 2.4 mg / dL. In the study 35.1 % had low calcium and low magnesium. 28.7 % had low calcium and normal magnesium. 1.1 % low calcium and increased magnesium. 9.6 % had normal calcium and low magnesium. In our study 78.72 % had no precipitating factors for seizures among them. Mean serum calcium was observed to be 8.39 ± 0.45 mg / dL and mean serum magnesium was observed to be 1.76 ± 0.27mg / dL.

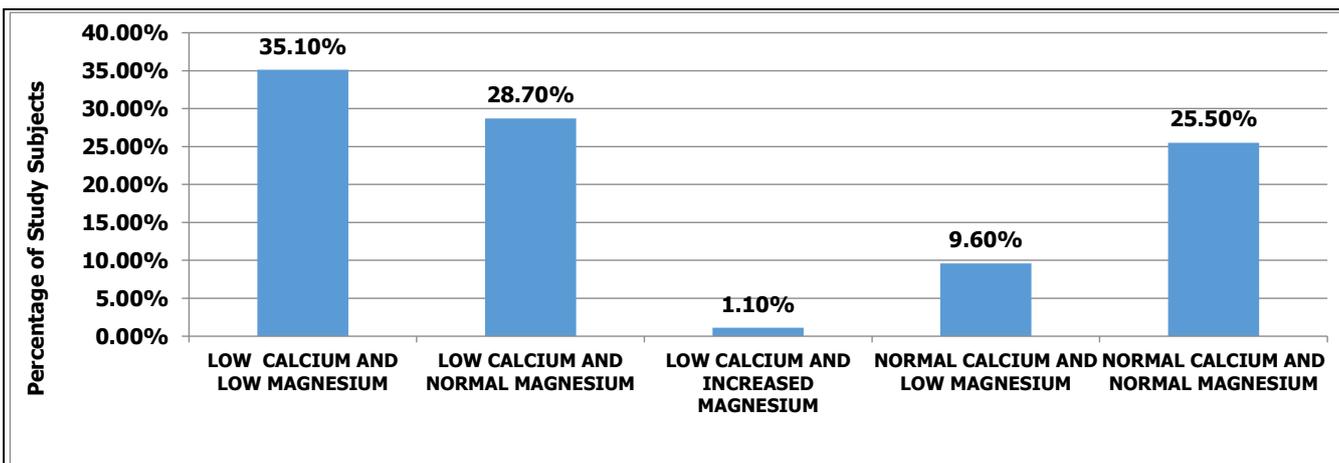


Figure 4. Classification of Percentage of Study Subjects with Low Calcium and Low Magnesium, Low Calcium and Normal Magnesium, Normal Calcium and Low Magnesium, Normal Calcium and Normal Magnesium Values

DISCUSSION

The most common cause of epilepsy is now believed to be genetic in origin. Even seizures in known epileptic patients can only be explained by subtherapeutic antiepileptic drug levels 60 % of the time. In present study mean total serum calcium was 8.36 ± 0.45 mg / dL. This is similar to the study done by Jassim et al.¹² in which mean total serum calcium was 8.4 ± 0.46 mg / dL. In Prasad et al.⁶ mean serum total calcium was comparatively very low 7.4 ± 1.32 mg / dL and was comparatively high in Chavan et al. 11.71 ± 0.98 mg / dL. In Sood et al.¹³ study, significant rise in serum calcium level was observed in idiopathic generalized tonic-clonic seizures (GTCS)

Study	Type of Calcium	Mean Serum Calcium (mg/dL)
Jassim et al.	Total calcium	8.4 ± 0.46
Sinert et al.	Ionised calcium	1.25 ± 0.07
Prasad et al.	Total calcium	7.4 ± 1.32
Jamil et al.	Total calcium	8.52 ± 0.96
Abdullahi et al.	Total calcium	9.2 ± 0.52
Chavan et al.	Total calcium	11.71 ± 0.98
	Ionised calcium	5.62 ± 0.53
Our study	Total calcium	8.36 ± 0.45

Table 1. Serum Calcium Level in Different Studies

Study	Type of Magnesium	Mean Serum Magnesium(mg / dL)
Jassim et al.	Total magnesium	1.64
Sinert et al.	Ionised magnesium	1.31 ± 0.14
Sinert et al.	Total magnesium	1.99 ± 0.26
Ramakrishna et al.	Total magnesium	0.964 ± 0.58
Prasad et al.	Total magnesium	1.67 ± 0.31
Jamil et al.	Total magnesium	1.97 ± 0.36
Abdullahi et al.	Total magnesium	1.8 ± 0.29
Chavan et al.	Total magnesium	1.72 ± 0.98

Table 2. Serum Magnesium Levels in Different Studies

In our study 64.9 % had total serum calcium less than 8.5 mg / dL. In Ramakrishna et al.¹⁴ it was 18 % and in Jamil et al.⁶ it was 41.4 %. In the present study, mean calcium was comparatively high in 21 - 30 years' subjects and comparatively low in 41 - 50 years subjects.

In Jassim et al.¹² study total serum calcium was significantly lower in epileptic patients. When estimated according to the age of patients, lowest value was seen in > 30 years 8.15 ± 0.389 mg / dL. In Prasad et al.⁶ no significant difference was observed between serum levels of calcium among different age groups.

In present study, mean serum calcium in males was 8.33 ± 0.47 mg / dL and in females was 8.39 ± 0.41 mg / dL. In Jassim et al.¹² study there was no significant variation in total levels of calcium between male 8.35 ± 0.527 mg / dL and female 8.45 ± 0.783 mg / dL epileptic patients. In Prasad et al.⁶ study significant difference was observed in serum calcium between males 7.6 ± 1.28 mg / dL and females 7.12 ± 1.2 mg / dL.

Among males and female's distribution of serum calcium below 8.5 mg / dL in Jamil et al.⁶ study was 37.5 % and 43.4 % respectively. In our study there was no significant difference between serum calcium levels and gender which was also a similar finding with Jassim et al.¹² study.

Mean serum magnesium in our study was 1.79 ± 0.28 mg / dL which was similar with Abdullahi et al.¹⁵ study 1.8 ± 0.29 mg / dL. Mean serum total magnesium in Jassim et al.¹²

was 1.64 mg / dL, in Sinert et al.⁵ was 1.99 ± 0.26 mg / dL, in Ramakrishna et al.¹⁴ was 0.964 ± 0.58 mg / dL, in Prasad et al.⁶ was 1.67 ± 0.3 mg / dL, in Jamil et al.⁶ was 1.97 ± 0.36 mg / dL, in Chavan et al. was 1.72 ± 0.98 mg / dL. In Sood et al.¹³ study significant reduction in serum magnesium was observed in idiopathic GTCS seizures. In our study 44.7 % had serum magnesium of < 1.8 mg / dL.

In the present study there was no significant difference in mean magnesium levels with respect to age distribution, mean magnesium was comparatively high in 41 - 50 years' subjects and comparatively low in 51 - 60 years' subjects. Ramakrishna et al.¹⁴ study there was no significant difference between serum magnesium and age. In Prasad et al.⁶ no significant difference was observed between serum levels of magnesium among different age groups. In our study there was no significant difference in mean magnesium levels with respect to age distribution which was similar finding with Ramakrishna et al.¹⁴

In present study females have mean magnesium of $1.78 \pm .26$ mg / dL and males have mean magnesium of $1.80 \pm .29$ mg / dL, there was no significant difference in mean magnesium with respect to gender which was similar with Jassim et al.¹² study where there was no significant variation in total levels of magnesium between males 1.5 ± 0.422 mg / dL and females 1.85 ± 0.63 mg / dL in epileptic patients. In Ramakrishna et al.¹⁴ study there was no significant difference between serum magnesium and gender. Prasad et al.⁶ no significant difference observed in serum magnesium between males and females. In Jamil et al.⁶ study serum magnesium was less than 1.8 mg / dL in 10 % and distribution among males and females was 8.3 % and 10.8 % respectively. In our study 35.1 % had both low calcium and magnesium, 28.7 % had low calcium and normal magnesium, 1.1 % had low calcium and increased magnesium, 9.6 % had normal calcium and low magnesium, 25.5 % had normal calcium and normal magnesium. Ramakrishna et al.¹⁴ study 18 % of subjects had both low calcium and magnesium. In Chavan et al. study variation between serum magnesium and calcium showed inverse relationship. In our study 78.72 % had no precipitating factors for seizures, among them mean serum calcium was observed to be 8.39 ± 0.45 mg / dL and mean serum magnesium was observed to be 1.76 ± 0.27 mg / dL.

There was significant difference in mean serum calcium with respect to number of episodes. Mean serum calcium was high among those with one episode ($8.57 \pm .26$ mg / dL) and low among those with 4 episodes of epilepsy ($7.58 \pm .39$ mg / dL), suggesting that there was decrease in mean serum calcium with respect to number of episodes. There was no significant difference in mean magnesium with respect to number of episodes.

CONCLUSIONS

Epilepsy is one of the most serious neurological conditions and has an impact not only on the affected individual but also on the family and indirectly on the community. Serum calcium and magnesium levels which play a role in seizure

initiation should be measured in all idiopathic epilepsy patients with breakthrough seizures as a seizure trigger.

Health-related quality of life scores is significantly lower in patients with epilepsy than in the general public and seizure free period on anti-epileptic drug therapy is a good predictor of quality of life. Breakthrough seizures in known idiopathic epileptic patients with good drug compliance and no precipitating factors can only be explained by sub-therapeutic antiepileptic drug levels 60 % of the time therefore considering the role of calcium and magnesium in the pathophysiology of seizures and by evaluating the results from the present study, serum calcium and magnesium levels need to be periodically monitored in all idiopathic epilepsy patients with good anti-epileptic drug adherence. Patients with low calcium and magnesium levels need supplementation which would help in controlling break through seizures in idiopathic epilepsy.

Data sharing statement provided by the authors is available with the full text of this article at jebmh.com.

Financial or other competing interests: None.

Disclosure forms provided by the authors are available with the full text of this article at jebmh.com.

REFERENCES

- [1] Mula M, Sander JW. Psychosocial aspects of epilepsy: a wider approach. *BJP Sych Open* 2016;2(4):270-274.
- [2] Leidy NK, Elixhauser A, Vickrey B, et al. Seizure frequency and the health-related quality of life of adults with epilepsy. *Neurology* 1999;53(1):162-166.
- [3] Chalasani S, Kumar MR. Clinical profile and etiological evaluation of new onset seizures after age 20 years. 2015;14(2):97-101.
- [4] Amaravathi KS, Nagamani R, Sakuntala P, et al. A study on clinical profile of new onset focal seizures in a tertiary care centre. 2015;5(7):5-8.
- [5] Sinert R, Zehtabchi S, Desai S, et al. Serum ionized magnesium and calcium levels in adult patients with seizures. *Scand J Clin Lab Invest* 2007;67(3):317-326.
- [6] 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.
- [7] Mathern GW, Pretorius JK, Kornblum HI, et al. Human hippocampal AMPA and NMDA mRNA levels in temporal lobe epilepsy patients. *Brain* 1997;120(Pt 11):1937-1359.
- [8] MacDermott AB, Mayer ML, Westbrook GL, et al. NMDA-receptor activation increases cytoplasmic calcium concentration in cultured spinal cord neurones. *Nature* 1986;321(6069):519-522. [Published erratum appears in *Nature* 1986 Jun 26-Jul 2;321(6073):888].
- [9] Heinemann U, Hamon B. Calcium and epileptogenesis. *Exp Brain Res* 1986;65(1):1-10.
- [10] Jamil U, Badshah M, Nomani AZ, et al. Serum calcium and magnesium abnormalities in patients with status epilepticus: a single centre tertiary care experience. *Pakistan J Neurol Sci* 2015;10(6):2012-2015. <http://ecommons.aku.edu/pjns>
- [11] Weisleder P, Tobin JA, Kerrigan JF 3rd, et al. Hypomagnesemic seizures: case report and presumed pathophysiology. *J Child Neurol* 2002;17(1):59-61.
- [12] 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.
- [13] Sood AK, Handa R, Malhotra RC, et al. Serum, CSF, RBC & urinary levels of magnesium & calcium in idiopathic generalised tonic clonic seizures. *Indian J Med Res* 1993;98:152-154.
- [14] RamaKrishna C, Basha SJ, VenkateswaraRao B, et al. Serum magnesium levels in seizure disorders. *J Evol Med Dent Sci* 2014;3(35):9313-9319.
- [15] Abdullahi I, Watila MM, Shahi N, et al. Serum magnesium in adult patients with idiopathic and symptomatic epilepsy in Maiduguri, Northeast Nigeria. *Niger J Clin Pract* 2019;22(2):186-193.