

SERUM MAGNESIUM LEVELS IN SEIZURE DISORDERSC. Rama Krishna¹, S. J. Basha², B. Venkateswara Rao³, B. Preethi⁴**HOW TO CITE THIS ARTICLE:**

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ABSTRACT: AIM: The objective of this study is to estimate the serum magnesium levels in seizure disorders and its possible association with the occurrence of seizures. Blood sample for serum magnesium and other electrolytes (blood glucose, potassium, sodium, calcium, chloride) were taken during the period from the onset of seizures up to 72 hours. **DESIGN:** The present study is a prospective study carried out at King George Hospital, Visakhapatnam. **MATERIALS & METHODS:** The present study was carried out on 50 subjects diagnosed as seizures (Generalized Tonic Clonic Seizures) in the age group of 20 to 60 years. The study also included 50 healthy subjects who are matched with cases. **STATISTICAL ANALYSIS:** The analysis was done using MS Office, Excel Sheet 2007 Software. **RESULTS:** Serum magnesium levels decreased significantly in patients with seizure disorders when compared to controls. (Mean values for Serum, Magnesium in cases vs. controls 0.964 vs. 2.038 mg/DL. The mean value for serum magnesium is lower when time elapsed after last seizure is shorter. **CONCLUSION:** Magnesium levels decreased in patients with seizure disorders and the mean values were lower when time elapsed since onset of seizure is shorter indicating the role of magnesium in the pathophysiology of seizures.

KEYWORDS: Serum Magnesium, Seizure disorders, Serum Electrolytes, Blood glucose.

INTRODUCTION: A seizure (from the latin scire, 'to take possession of) is a paroxysmal event due to abnormal, excessive, hypersynchronous discharges from an aggregate of CNS neurons.¹ Seizures can vary from the briefest lapses of attention or muscle jerks to severe and prolonged convulsions. Seizures increase a person's risk of premature death by about 2 or 3 times compared to the general population. The incidence rate varies from 38 to 49.3 to 1 lakh population per year in India.²

Causes of seizure disorders vary according to different age groups¹. Trauma, cerebrovascular accidents, brain tumors from some of the causes in older age groups. The various types of seizures include simple partial seizures, complex partial seizures, generalized seizures, myoclonic seizures and grandmal seizures.

CT scan, MRI, EEG form important tools for diagnosing seizures apart from the parameters estimated in the present study. The normal adult human body contains 1000 mmol of magnesium, which is distributed in bones, skeletal muscle, soft tissues and extracellular fluid in varying proportions. The normal serum magnesium 1.6 to 2.5 mg/dl.

Neuronal excitability is regulated by the balance between excitatory and inhibitory influences, both intrinsic and synaptic. Epileptic events consist of giant excitatory post synaptic potentials which are manifestations of synchronous burst firing of many neurons.³

Magnesium is an essential cofactor for many enzymatic reactions, especially those involved in energy metabolism.⁴ Magnesium results in state of neuronal hyper excitability convulsions and various psychiatric symptoms. AMPA and Kainite receptors mediate fast excitatory transmission. NMDA receptors⁵ mediate prolonged phase of excitatory neurotransmission.

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Activation of AMPA/ Kinase receptors depolarize the neuronal cell membrane, releasing the magnesium block of the NMDA receptor. With the removal of magnesium block, NMDA receptors, which are colocalised with AMPA receptor, become activated. The GABA A⁶ and GABA B receptors, which are inhibitory in nature, also play an important role in the pathophysiology of seizures. CT, MRI, EEG are important tools in the diagnosis¹ of seizures apart from the parameters estimated in the present study.

MATERIALS AND METHODS:

Patients: The present study was conducted on fifty patients diagnosed as seizures (generalized, tonic clonic seizures, GTCS), admitted in KGH, Visakhapatnam. The inclusion criteria included seizure patients in the age group between 20 to 60 years, irrespective of gender and diagnosed as GTCS and time elapsed since onset of seizure was less than 72 hours. The exclusion criteria included subjects with age less than 20 and more than 60 years. All patients with more than 72 hours from onset of seizures were excluded.

The present study was done over a period of 6 years from 2008 to 2014 in the medicine wards of King George Hospital, Andhra Medical Collage, Visakhapatnam after taking permission from the principal of Andhra Medical Collage, Visakhapatnam (Ethics Committee). The patients were examined by taking a detailed history, physical and neurological examination was done by the faculty members of the medical wards. Written and informed consent was taken from the patients and control subjects. Venous samples were collected from the patients and control subjects for estimation of serum magnesium, calcium, potassium, chloride, and blood glucose.

Reference range of parameters estimated:

Serum Magnesium: 1.8 to 2.5 mg/dl

Serum Calcium: 9 to 11 mg/dl

Serum Potassium: 3.5 to 5 meq/L

Sodium: 136 to 145 meq/L

Blood Glucose: 110 to 140 mg/dl

Methods of estimation:

Magnesium: Magnesium in the serum was estimated by Calmagite method.

Calcium: Calcium in the serum was estimated by Ortho cresolphthalein complexone method.

Glucose: Glucose in the venous blood was determined by the glucose oxidase method.

Chloride: Chloride in blood estimated by mercuric thiocyanate method.

Sodium & Potassium were estimated in serum by flame photometry at Central lab KGH, Visakhapatnam.

RESULTS:

Study Subjects:

Magnesium: The mean serum Mg in the study group in 0.964 ± 0.58 mg/dl. And in the control group is 2.038 ± 0.279 mg/dl. Significant hypomagnesaemia is seen in 40 out of 50 cases. The p value is significant with less than 0.001.

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The duration from onset of seizure in 40 patients was less than 6 hours. 4 out of the remaining 10 had near normal serum magnesium levels. The duration from the onset of seizure was 48 hours.

Six patients whose duration from onset of seizure was 72 hours, the serum magnesium level was normal limits.

Age group	CASES			CONTROLS		
	Male	Female	Total	Male	Female	Total
21-30	07 (14.00)	02 (04.00)	09 (18.00)	06 (12.00)	05 (10.00)	11 (22.00)
31-40	10 (20.00)	04 (08.00)	14 (28.00)	10 (20.00)	03 (06.00)	13 (26.00)
41-50	11 (22.00)	03 (06.00)	14 (28.00)	10 (20.00)	02 (4.00)	12 (24.00)
51-60	09 (18.00)	04 (08.00)	13 (26.00)	09 (18.00)	05 (10.00)	14 (28.00)
Total	37 (74.00)	13 (26.00)	50 (100.0)	35 (70.00)	15 (30.00)	50 (100.0)

Table No. 1: Showing Distribution of study population according to age group & sex (N1=50, N2 = 50)

Mean age of the cases is 41.6 ± 10.22 years of SD. Mean age of the controls is 41.3 ± 10.90 years. There is no significance difference between these two groups $t = 0.14$, $d.f = \infty$ with P value of $P > 0.05$.

Parameter	Cases	Controls
Sample Size(N)	50	50
Mean	0.964	2.038
SD	0.580	0.279
Mean difference	-1.074	-----
SE difference	0.090	-----
t value	11.93	-----
Degrees of Freedom	∞	
P value	$P < 0.001$	Highly Significant

Table No. 2: Showing Serum Magnesium levels compared in both the groups (N1= 50, N2 = 50)

The Magnesium levels in both the groups differ significantly $P < 0.001$

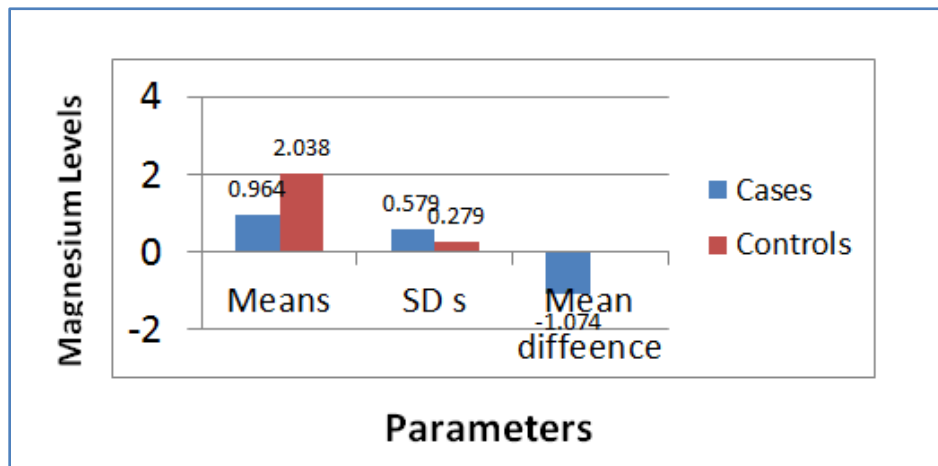


Fig. 1: Comparison of Magnesium Levels B/W Cases and Controls

	No. of Cases	%
SERUM CALCIUM (8.5 - 11 mg/dl)	41	82
SERUM CALCIUM (<8.5 mg/dl)	9	18

Table 3: Serum calcium levels in cases. 82% are in Normal range and 18% are in below normal range

	No. of Cases	%
SERUM POTASSIUM (3.5 - 5 mmol/l)	45	90
SERUM POTASSIUM (<3.5 mmol/l)	5	10

Table 4: Serum potassium levels in cases. 90% are in normal range and 10% are in below normal range

DISCUSSION: The present study was conducted on fifty cases of seizure disorder admitted in King George Hospital, Vishakapatnam and fifty controls in the age group ranging from 20 to 60 yrs.

Of the fifty cases, thirty-seven (37) are males and thirteen (13) are females. There is no variation of Serum Magnesium levels with respect to age and gender. In controls the Serum Magnesium is in the normal range. The values of mean and SD in cases are 0.969 & 0.580 whereas in controls it is 2.038 & 0.279 respectively.

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In the study group which consisted of fifty (50) cases, forty cases (80%) showed significant lower Magnesium levels. All these patients had duration of <6hrs from onset of last seizure. Out of the other ten cases four cases (8%) showed near normal levels of Serum Magnesium levels.

These cases had duration of 48 hrs. from onset of last seizure. The remaining six cases (12%) had normal levels of Serum Magnesium who were 72 hours from the onset of last seizure.

In the study out of fifty (50) cases, serum calcium in 41 cases (82%) and serum Potassium in 45 cases (90%) had levels in the normal range. Ionic calcium is known to be most active and its deficiency is responsible for symptoms like muscle twitchings tetany, seizures, etc. The mean calcium level in cases (<8.5 mg/dl group) is 8.1 ± 0.173 mg/dl and in cases (more than 8.5 to 11 mg/dl group) is 9.15 ± 0.277 .

Out of the 50 cases 41 had a normal serum calcium level and 9 cases (18%) had levels in less than normal range. The mean potassium in cases (<3.5 mmol/L group) is 3.24 ± 0.13 mmol/L and in cases (more than 3.5 to 5 mmol/L group) is 4.34 ± 0.288 . Out of 50 cases, 45 cases had a normal serum potassium level and in 5 cases had levels in less than normal range.

Serum Calcium⁷ in 9 cases (18%) and serum potassium in 5 cases (10%) had levels less than normal, all of which are associated with serum hypomagnesemia and all are <6 hours from onset of last seizure. In controls these parameters fell in the normal range.

The mean sodium level in cases is 141.46 ± 3.29 mmol/L and in controls is 140.24 ± 2.74 mmol/L. The mean serum chloride level in cases is 101.84 ± 2.87 mmol/L and in controls is 102.56 ± 2.51 mmol/L. The mean random blood glucose level in cases is 122.98 ± 10.93 mg/dL and in controls is 122.80 ± 10.39 mg/dL.

Although hyponatremia and hypoglycemia are known to cause seizures, these parameters, i.e. serum sodium, serum chloride, serum glucose did not show much difference between cases and controls and had Mean values in the normal range.

In the study conducted by Horaciom Canelas, ⁸ Luimarquesdeassis and Dejorge, 1965, the results showed the existence of hypomagnesemia in seizures (p value <0.001) and the magnesium level was lower when time elapsed after convulsion was shorter. The present study is also in accordance with the above study.

In a study conducted by Oladipo OO, Ajala MO, Okubadejo N¹¹ in 2003 Dec. Plasma Magnesium levels were estimated in adult patients with seizures using Calmagite dye colorimetric method. In their study 45 adults with seizures and 35 controls were taken. The Mean plasma Magnesium in the patients was significantly lower than that obtained in the controls (P<0.001). The present study is correlated with the above study showing lower Magnesium levels than that in controls. (P value<0.0001).

In the study conducted by Rajarathinam, and Justin of Madurai Medical College estimated Serum Magnesium level in fifty cases and fifty controls. Serum Mg level in cases showed magnesium lower than that in controls which was independent of age, gender and EEG changes. Serum Magnesium increased significantly from postictal to 72 hrs.

The present study is in accordance with the above study showing Serum Magnesium levels lower than that in controls. The present study also included patients who had a duration of last seizure of 48hrs to 72hrs (approx.) and these patients also had Serum Magnesium in the normal range.

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As a limitation we have not compared the findings of the above parameters with the patients CT scan and EEG which are considered the gold standard in the diagnosis of seizure disorders. From the above findings, it is clear that hypomagnesaemia is an important risk factor in the causation of seizures. Also along with hypomagnesaemia, hypokalaemia and hypocalcaemia may also play a role in the causation of seizures.

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CONCLUSIONS & RECOMMENDATIONS: Serum Magnesium levels decreased significantly in patients with seizure disorder when compared to the controls (Mean value for serum magnesium in cases vs. controls is 0.964 vs. 2.038mg/dl). Hence it may be useful for evaluation of patients with Seizure disorder. The Mean value for serum magnesium is lower when time elapsed after last seizure is shorter. Hence it may be used as a prognostic index (In all cases with <6 hrs. duration the Mean value is 0.693).

Considering the role of magnesium in the pathophysiology of seizures and by evaluating the results from the present study, magnesium may be used for treatment of intractable seizures. There is no significant relationship in patients with seizure disorder between serum magnesium levels and age and gender. In 18% cases there is associated hypocalcaemia with hypomagnesaemia¹¹ and in 10% cases there is associated hypokalaemia with hypomagnesaemia indicating the importance of estimating these parameters also in patients with seizure disorder.

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