

# Understanding the Effects of Serum Magnesium Levels in Cases of Acute Ischemic Stroke- A Hospital Based Case Control Study from North Eastern India

Sanjeeb Roy<sup>1</sup>, Kallol Bhattacharjee<sup>2</sup>, Nabaruna Paul<sup>3</sup>

<sup>1</sup>Postgraduate Trainee, Department of General Medicine, Silchar Medical College and Hospital, Assam, India.

<sup>2</sup>Professor, Department of General Medicine, Silchar Medical College and Hospital, Assam, India.

<sup>3</sup>Postgraduate Trainee, Department of General Medicine, Silchar Medical College and Hospital, Assam, India.

## ABSTRACT

### BACKGROUND

Stroke or cerebrovascular accident is defined as an abrupt onset of a neurologic deficit that is attributable to a focal vascular cause. It is the second most common cause of mortality in the world. Magnesium is one of the most important and clinically significant intracellular bivalent cations. The possible explanations by which magnesium brings down the risk of ischemic cerebral infarction involve an improvement in endothelial function and also the inhibition of platelet aggregation. We wanted to estimate the serum magnesium levels in acute ischemic stroke, predict the neurological outcome in patients of acute ischemic stroke and evaluate its correlation with serum magnesium levels.

### METHODS

This study was conducted in the Department of General Medicine, Silchar Medical College and Hospital for a duration of 18 months. This is a case control study that included 126 cases of acute ischemic stroke and an equal number of age and sex matched healthy controls. The serum magnesium was estimated using a VITROS 5600 autoanalyzer.

### RESULTS

The highest incidence of Acute Ischemic Stroke was observed in the age group of 50-69 years with an overall male preponderance of ischemic stroke. The mean serum magnesium level was significantly lower in cases as compared to controls ( $p < 0.05$ ) and patients with lower serum magnesium levels had a higher mean MRS score at discharge or death.

### CONCLUSIONS

Serum magnesium level is an independent risk factor for acute ischemic stroke. Low serum magnesium levels in ischemic stroke patients on admission were strongly associated with a poorer neurological outcome.

### KEYWORDS

Cerebrovascular Accident, Stroke, Magnesium, Acute Ischemic Stroke, Risk Factor, Discharge

*Corresponding Author:*

*Dr. Kallol Bhattacharjee,*

*Professor,*

*Department of General Medicine,*

*Silchar Medical College and Hospital,*

*Silchar, Cachar- 788014, Assam, India.*

*E-mail: kbsilchar64@gmail.com*

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## BACKGROUND

A stroke or cerebrovascular accident is defined as an abrupt onset of a neurologic deficit that is attributable to a focal vascular cause.<sup>1</sup> It is the 2<sup>nd</sup> most common cause of mortality in the world.<sup>1</sup> Stroke is mainly divided into two types – Ischemic and Haemorrhagic. Stroke is a major factor leading to disability among the elderly population. The mortality of stroke patients in the acute phase is as high as 20%.<sup>2</sup> In India the incidence of stroke is 119-145/100,000.<sup>3</sup> However the prevalence of stroke in our nation is 84-262/100,000 in the rural and 334-424/100,000 in the urban areas.<sup>3</sup> When an intracranial vessel is occluded, it leads to a reduction in the flow of blood to the part of the brain that the vessel supplies.<sup>4</sup> If the cerebral blood flow becomes nil, death of the brain tissue occurs in 4-10 minutes.<sup>4</sup> Magnesium (Mg) is regarded as an important and clinically significant intracellular bivalent cation.<sup>5</sup> Along with calcium, normal concentrations of extracellular magnesium are crucial to maintain normal neuromuscular activity.<sup>5</sup> Owing to the ability of intracellular magnesium to form an important complex with ATP, it definitely is an extremely important cofactor for various enzymes, transporters and nucleic acids that are required for normal cellular functioning, replication, and energy metabolism.<sup>5</sup> Normal concentration of Magnesium is 0.7- 1 mmol/l or 1.7 – 2.4 mg/dL.<sup>5</sup> Magnesium is a physiological calcium channel antagonist which helps in regulating blood pressure, vasomotor tone and peripheral blood flow.<sup>6</sup> Magnesium is an important mineral which has been observed to exhibit neuroprotective properties in experimental studies. The possible explanations by which magnesium brings down the risk of ischemic cerebral infarction involve an improvement in endothelial function and also the inhibition of platelet aggregation.<sup>7</sup>

Despite the substantial progress in modern medicine along with the advent of newer diagnostic as well as therapeutic modalities, stroke is still considered to be a global health problem as well as a national health concern thus raising the possibility of the presence of some unknown or underestimated risk factors. So the current scenario demands the identification of certain bio-markers in patients of acute ischemic stroke which can impact the neurological outcome thus carrying a definite prognostic value.

We wanted to estimate the serum magnesium levels in acute ischemic stroke, predict the neurological outcome in patients of acute ischemic stroke and evaluate its correlation with serum magnesium levels.

## METHODS

This study was conducted in the Department of General Medicine, Silchar Medical College & Hospital, Silchar, Assam. This was a single centered case control study. The duration of this study was of 18 months done from 1<sup>st</sup> May 2018 to 31<sup>st</sup> October 2019. 126 consecutive cases with acute ischemic stroke satisfying the inclusion criteria during the entire study period who were admitted to Silchar Medical

College and Hospital (SMCH) and an equal amount of healthy controls who were age and sex matched had been selected for participation in the study.

### Inclusion Criteria

- 1) Age > 18 years.
- 2) Patients with focal or global neurologic deficit.
- 3) CT Brain proved cases of acute ischemic stroke.

### Exclusion Criteria

- 1) CT Brain showing haemorrhagic stroke.
- 2) Patients with a known or possible source of a cardiac emboli (atrial fibrillation, valvular heart disease and those on prior anticoagulation therapy).
- 3) Past history of vascular disease (previous stroke, angina, myocardial infarction, peripheral vascular disease)
- 4) Patients on drugs affecting serum magnesium levels (loop and thiazide diuretics, long term PPI use like Omeprazole, Antacids containing magnesium, antimicrobials like Amphotericin B and Pentamidine, Digitalis, Cyclosporine, Cisplatin and Mycophenolate mofetil).
- 5) Renal and Liver diseases
- 6) Malignancy
- 7) Chronic alcoholism

Subjects for the control group were selected randomly from different sections of the society belonging to diverse socio-economic status who otherwise appeared healthy. The members of this group didn't complain of any symptoms related to vascular diseases or other neurological illness. The subjects selected for the study comprised of individuals who were matched for age and sex with the case group. The control group comprised of 126 subjects. All individuals of the control group cooperated voluntarily, and an informed consent was taken.

NCCT (Non Contrast Computed Tomography) scan of brain was done for diagnosis of acute ischemic stroke cases. All the cases were evaluated using Philips 128 slice ingenuity elite CT scanner. Serum magnesium was estimated using the VITROS 5600 Integrated System auto analyser.

### Ethical Considerations

Informed consent was taken from all the study participants. Clearance from the ethical committee of SMCH was obtained.

## RESULTS

The study subjects were investigated by various radiological and biochemical tests besides a comprehensive clinical examination and results were analysed by using Chi Square test and Student's T-test, which was two tailed. In all analyses, a p-value of <0.05 was considered to be statistically significant. SPSS version 20 was used for all statistical analyses. The youngest case was aged 25 years and the oldest case was aged 99 years whereas in the

control group they were 24 years and 96 years respectively. There were 82 males and 44 females in both the study groups. The male to female ratio was 1.86:1.

Out of the cases 82 were smokers and in the control group 58 were smokers. There was significant difference observed in the smoking habits of the cases and controls ( $p < 0.05$ ). However, no significant difference was observed in the alcoholic habits and sedentary lifestyle habits of the cases and controls ( $p > 0.05$ ). In this study 63.5% of the cases and 57.1% of the controls were hypertensives (as per AHA 2017 guidelines) with no significant difference of the hypertensive status of cases and controls. The present study also did not show any kind of significant difference in the diabetic status of the cases and controls. In the present series the commonest presenting complaint was hemiparesis/hemiplegia seen in 79.4% of cases followed by speech disturbances seen in 68.2% of cases. In the present study a statistically significant difference was observed in the mean serum Mg levels of the cases and controls ( $p < 0.05$ ).

Age Interval in Years	No. of Cases	No. of Controls
<29	1	1
30 – 39	3	3
40 – 49	22	22
50 – 59	31	31
60 – 69	43	43
70 - 79	19	19
80 - 89	5	5
>90	2	2
TOTAL	126	126

**Table 1. Age-Wise Distribution of the Subjects in Both Cases and Controls**

Sex	Cases	%	Controls	%
Male	82	65	82	65
Female	44	35	44	35
Total	126	100	126	100

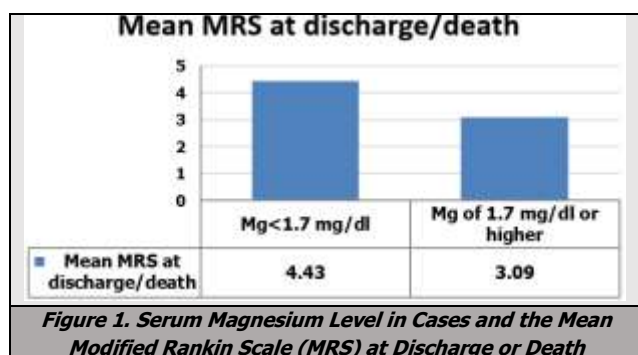
**Table 2. Gender-Wise Distribution of the Subjects in Both Cases and Controls**

	Cases	Controls	p value
	Mean ± SD	Mean ± SD	
S. Magnesium (mg/dL)	1.62±0.2	1.81±0.2	<0.05

**Table 3. Comparison of Serum Magnesium in Cases and Controls**

	Mg < 1.7 mg/dL	Mg ≥ 1.7 mg/dL
No. of Cases	75	51
Percentage	59.5	40.5

**Table 4. Level of Serum Magnesium in Cases**



Almost 60% of the patients presenting with acute ischemic stroke had their serum Mg levels below the normal value. Out of the 126 cases of acute ischemic stroke, 11

cases (8.7%) expired within one week of hospitalisation. The remaining cases had a partial neurological improvement and were discharged after the hospital stay of 1 week.

## DISCUSSION

In the study population, 58.7% of the acute ischemic stroke cases were aged between 50-69 years. Kaur Jaspreet ET al<sup>8</sup> also observed highest number of patients (58%) who were the aged between 50-69 years. In the present series males were affected more by acute ischemic stroke. Of all the cases in our study, 65% were males and 35% were females and the male to female ratio was 1.86:1. It is comparable to the following studies-

Studies	M:F ratio
Kaur Jaspreet et al <sup>8</sup>	1.17:1
Zafar Faleha et al <sup>9</sup>	1.16:1
Behera et al <sup>10</sup>	1.86:1
Alia Saberi et al <sup>11</sup>	1.57:1
Present study	1.86:1

**Table 5. Comparison of M:F Ratio**

In this study, the prevalence of hypertensive cases was 63.5%. This result correlates with findings by Paranthkan et al,<sup>12</sup> Behra et al, You S et al<sup>13</sup> and Koppula et al.<sup>14</sup> However Harpreet Singh et al<sup>15</sup> found only 32% hypertensives in their study.

Studies	Prevalence of Hypertension
Paranthkan et al	66%
Behra et al	59%
Koppula et al	55%
Harpreet Singh et al	32%
You S et al	78%
Present study	63.5%

**Table 6. Prevalence of Hypertension in Various Studies**

In this study, 65% of the cases were smokers. Koppula et al found the prevalence of smokers at 40.7%. Results seen in other studies by Paranthkan et al, You S et al and Behera et al found the prevalence of smoking at 33%, 18% and 28% respectively. The relatively higher prevalence of smoking habits observed in this study is probably an indirect indicator of the high smoking burden in this part of the country which has put the population at a high risk of suffering from smoking related illness including stroke. In this study, serum Mg levels in the cases and controls were compared and it was observed that the mean serum Mg level in the cases was significantly lower (1.62±0.2 mg/dL) than in the control group (1.81±0.2 mg/dL) with a p-value of <0.05.

Similar results have been observed in other studies. According to a study by Cojocar IM et al<sup>16</sup> in the year 2007, mean serum magnesium in cases was seen to be lower than in controls. In the study by Khalid Md Khan et al<sup>17</sup> the mean serum Mg level in patients suffering from acute ischemic stroke was 1.71±0.51 mg/dL. In another study by RK Patel et al<sup>18</sup> which considered ischemic as well as haemorrhagic stroke, the mean serum Mg level in patients of ischemic stroke was 1.72±0.74 mg/dL. However, in another Indian study done by Kaur Jaspreet et al it was observed that the

mean serum Mg level in patients suffering from ischemic stroke was  $2.05 \pm 0.48$  mg/dL.

In this study it was observed that the mean MRS of the cases at discharge or death with subnormal levels of serum magnesium ( $<1.7$  mg/dL) was 4.43 which was higher compared to the mean MRS of 3.09 in the patients having serum magnesium of 1.7 mg/dL or higher. Similar results were observed in the study done by Alia Saberi et al, RK Patel et al and Khalid Md Khan et al which also showed a negative correlation of serum Mg levels and MRS at discharge or death. In another study done by You S et al published in 2017 it was observed that patients of stroke with lower serum magnesium levels had more severe stroke and a higher MRS and NIHSS score. The present study had a mortality of 8.7% in patients of acute ischemic stroke within a week of hospitalization. The mortality observed in the study done by Khalid Md Khan et al was 2.5%. However in other studies regarding acute ischemic stroke done by Behera et al and Harsh ET al<sup>19</sup> the mortality was seen to be at 9% and 8% respectively which is similar to the results observed in the present study.

### CONCLUSIONS

Lower level of serum Mg is an independent risk factor for acute ischemic stroke. Low serum magnesium level of the ischemic stroke patients on admission was strongly associated with a poorer neurological outcome. Cases with subnormal levels of serum magnesium had a higher mean MRS scoring at discharge or death than patients who had normal magnesium levels. Estimation of serum magnesium is a cost effective, easily available prognostic marker in the evaluation of the dreaded catastrophe in the form of acute ischemic stroke.

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