

## Original Research Article

# Serum magnesium levels in patients of ischemic stroke and its correlation with neurological disability

Vishali Kotwal\*, Rajesh Minia

Department of Medicine, Government Medical College, Jammu, Jammu and Kashmir, India

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**\*Correspondence:**

Dr. Vishali Kotwal,

E-mail: [thakuramit2277@gmail.com](mailto:thakuramit2277@gmail.com)

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### ABSTRACT

**Background:** Stroke is a leading cause of death and disability worldwide acute ischaemic stroke accounts for 87% of strokes and mostly affects persons at the peak of their lives. Magnesium is known to have neuroprotective effects in ischemic stroke through a variety of mechanisms including decrease in glutamate release and inhibition of NMDA receptors and vasodilation. Previous studies on serum magnesium levels in stroke patients have shown variable results with many of them finding lower levels than in normal subjects. This study was undertaken to compare serum magnesium levels in patients of acute ischemic stroke with those of controls and also find a correlation if any between serum magnesium levels and neurological disability.

**Methods:** This was a prospective non-interventional case-control study in which 50 patients of acute ischemic stroke in the age group of 20 to 80 years admitted in the department of Medicine Government Medical College Jammu from October 2019 to January 2020 were taken. Their serum magnesium levels were analysed within first 24 hours of admission and neurological disability was measured using modified Rankin Score. Serum magnesium levels were also estimated in 35 healthy controls for comparison.

**Results:** Serum magnesium was lower in the study group (mean of  $1.85 \pm 0.36$ ) as compared to the control group (mean of  $2.4 \pm 0.21$ ) which was statistically significant (p value = 0.001). Modified Rankin Score was 4 to 5 in 27 patients and 2 to 3 in 23 patients and it was negatively correlated with serum magnesium levels ( $r = -0.67$ ).

**Conclusions:** Ischemic stroke patients had lower serum magnesium levels as compared to healthy subjects in our study and also lower levels were seen in those with higher neurological disability.

**Keywords:** Ischemic stroke, Modified Rankin score, Neuroprotection, Serum magnesium

### INTRODUCTION

Stroke is a term used for focal neurological deficits and CNS injuries of vascular origin. Stroke is the second leading cause of death and third leading cause of disability worldwide.<sup>1</sup> Globally seventy percent of the stroke cases occur in low and middle income countries.<sup>2</sup> The cumulative incidence of stroke in India ranges from 105 to 152/100,000 persons per year, and the crude prevalence of stroke ranges from 44.29 to 559/100,000 persons in different parts of the country.<sup>3</sup> Stroke can be

divided into two major categories, ischaemic and haemorrhagic. Acute ischaemic stroke accounts for 87% of strokes. Stroke mostly affects persons at the peak of their lives. After stroke, there is decreased blood flow and subsequent disturbance in ionic homeostasis and intracellular edema. This leads to release of excitatory neurotransmitters and production of free radicals because of mitochondrial dysfunction. Neuroprotective treatments for acute ischemic stroke are targeted at the large array of cellular, biochemical and metabolic disturbances that occur after focal brain ischemia to prevent death of

ischemic penumbra and reduce the infarct size.<sup>4</sup> Among the various neuroprotective molecules tested in clinical trials are NMDA antagonists, uric acid, edaravone none of which showed any benefit and some had serious adverse effects.<sup>5-7</sup> Citicholine is one molecule which has shown a positive effect on cognition and functional status when given for a prolonged period of 1 year.<sup>8</sup> Another molecule is magnesium which has shown a promising effect in preclinical trials of ischemic stroke but its efficacy in clinical trials is conflicting.<sup>9</sup> Although role of dietary magnesium in decreasing risk of stroke and other cardiovascular diseases and death has been shown in many studies.<sup>10</sup> Therapeutic uses of magnesium include prevention of seizures in preeclampsia/eclampsia, and prevention of cardiac arrhythmias.<sup>11</sup>

Aim of this study was undertaken to compare the serum magnesium levels in patients of ischemic stroke and normal controls and also to find correlation between serum magnesium levels and neurological disability.

**METHODS**

This was a prospective non interventional case control study conducted in the department of Medicine Govt. Medical College Jammu on patients of acute ischemic stroke admitted in the department w.e.f October 2019 to January 2020. 50 patients who met the inclusion criteria were included in the study.

**Inclusion criteria**

- Patients with a clinical diagnosis of acute ischemic stroke
- Age between 20 and 80 years

**Exclusion criteria**

- Hemorrhagic stroke
- Previous stroke
- Cardioembolic stroke
- Seizure disorder
- Cardiac dysfunction
- Renal dysfunction
- Diabetes mellitus
- Patients on diuretics
- Pregnancy

A brief history and detailed neurological examination was done, CT scan of the brain was done and their serum magnesium levels were measured within 24 hours of presentation along with other routine investigations like complete blood count, random blood sugar, renal function tests, liver function tests, sodium, potassium and calcium. Modified Rankin Score was used to estimate the neurological disability of the patients. Scoring was done from 1 to 6. A score of 1 meant there was no significant disability despite symptoms and patient was able to carry out all usual duties and activities. A score of 2 meant

slight disability and patient was unable to carry out all previous activities but able to look after own affairs without assistance. A score of 3 was given to patients with moderate disability i.e requiring some help but able to walk without assistance. A score of 4 meant moderately severe disability i.e unable to walk and attend to bodily needs without assistance. A score of 5 meant severe disability i.e bedridden, incontinent and requiring constant nursing care and attention. A score of 6 was given to those who died. 35 normal controls of both the sexes in the same age group were also taken and their serum magnesium levels were measured for comparison.

**Statistical analysis**

Means and standard deviations of various variables were calculated in both controls and cases. Values were compared using t test which was used to calculate p value. A p value <0.05 was considered statistically significant. Pearson’s correlation coefficient was calculated to see the correlation between mRS and serum magnesium levels.

**RESULTS**

Mean age of the patients was 60.7 years with standard deviation of 11.7 and mean age of the controls was 55.8 with standard deviation of 14.5. There were 32 males and 18 females (male to female ratio was 1.8:1) in the study group and 20 males and 15 females in the control group (male to female ratio was 1.3:1).

**Table 1: Comparison of variables between cases and controls.**

Variables	Cases (no. 50 )	Controls (no. 35)	p value
	Mean±sd	Mean±sd	
Age (years)	60.7±11.7	55.8±14.5	0.156
Random blood sugar (mg%)	123±33.4	116±15.31	0.22
Serum calcium (mg%)	8.64±0.71	8.40±0.36	0.05
Serum magnesium (mg%)	1.85±0.36	2.4±0.21	0.001

**Table 2: Correlation between serum magnesium levels and mRS.**

Serum magnesium (mg%)	No. of patients (m RS )
1-1.5	10 (4)
	2 (5)
1.6 -2	4 (2)
	6 (3)
	10 (4)
	4 (5)
2.1-2.5	9 (2)
	3 (3)
2.5-3	1(4)
	1 (2)

Serum calcium and random blood sugar levels were comparable in both the groups. Serum magnesium was lower in the study group (mean of  $1.85 \pm 0.36$ ) as compared to the control group (mean of  $2.4 \pm 0.21$ ) which was statistically significant ( $p$  value = 0.001). (Table 1) Modified Rankin Score was 4 to 5 in 27 patients and 2 to 3 in 23 patients and it was negatively correlated with serum magnesium levels ( $r = -0.67$ ) (Table 2).

## DISCUSSION

In this study, authors found that serum magnesium levels were lower in stroke patients than in controls and also within the stroke group patients with higher neurological disability had a lower score than patients with a lower neurological disability. Magnesium possibly reduces neuronal damage in cerebral ischemia by various mechanisms including inhibition of ischemia induced glutamate release, NMDA receptor antagonism, blocking calcium entry into the cells, buffering of excessive calcium, preventing depletion of ATP and also by increasing cerebral blood flow.<sup>11</sup> Cojocaru et al, in their study found a similar result showing lower magnesium levels in patients of ischemic stroke as compared to controls and also a lower level in patients with higher degree of neurological disability Lampl Y et al, and Bayir A et al, found a significant correlation between lower CSF magnesium levels in patients of ischemic stroke and a severe neurological disability but not with serum magnesium levels.<sup>12-14</sup>

Ovbiagele et al, found no relation between admission serum magnesium levels and severity of stroke.<sup>15</sup> Saberi et al, in their study also found a reciprocal correlation between serum magnesium levels and neurological disability.<sup>16</sup> However, Siegler et al, found that acute decrease in serum magnesium level after ischemic stroke was not associated with a poor neurological outcome but it was a retrospective study and effect of confounding cannot be excluded and also they did not take renal function of the patients into consideration.<sup>17</sup> But even then they found a relationship between magnesium levels at baseline and magnesium replacement with NIHSS over time. The reason for these discrepancies may be due to factors that lead to changes in serum magnesium levels like fluid replacement during early hours of patient admission and diuretic use.

Thus benefits of magnesium in diet and role of magnesium in vascular health and neuroprotection are endorsed by many studies and in this study also authors found lower serum magnesium levels in patients of ischemic stroke as compared to healthy subjects and also it was seen that higher neurological disability was associated with lower serum magnesium levels. Further large-scale studies are required to compare the serial changes in serum magnesium levels between patients of ischemic stroke given intravenous magnesium and those not replaced with magnesium and see its effect on neurological disability.

## CONCLUSION

Ischemic stroke patients had lower serum magnesium levels as compared to healthy subjects in this study and also lower levels were seen in those with higher neurological disability. So, magnesium may have a role in neuroprotection and magnesium supplementation in patients with vascular risk factors may reduce the incidence of stroke and severity of stroke and also magnesium replacement in early phase of ischemic stroke may reduce the infarct size. Further studies are needed in this regard.

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