

#### **Original Research Article**

 Received
 : 27/08/2024

 Received in revised form
 : 12/10/2024

 Accepted
 : 28/10/2024

Keywords: Mg, Acute Ischemic Stroke, Serum Magnesium.

Corresponding Author: **Dr. C. Santhosh Kumar,** Email: csanthosh545@gmail.com

DOI: 10.47009/jamp.2024.6.5.147

Source of Support: Nil, Conflict of Interest: None declared

Int J Acad Med Pharm 2024; 6 (5); 772-775



# RELATIONSHIP BETWEEN SERUM MAGNESIUM CONCENTRATION AND SHORT-TERM OUTCOME IN ACUTE ISCHEMIC STROKE

C. Santhosh Kumar<sup>1</sup>, M.Praveen Kumar<sup>2</sup>, S. Kasipandian<sup>3</sup>

<sup>1</sup>Final Year Postgraduate, Department of General Medicine, Trichy SRM Medical College Hospital and Research Centre, Trichy

<sup>2</sup>Associate Professor, Department of General Medicine, Trichy SRM Medical College Hospital and Research Centre, Trichy

<sup>3</sup>Professor, Department of General Medicine, Trichy SRM Medical College Hospital and Research Centre, Trichy

#### Abstract

Background: Magnesium (Mg) has a notable impact on the vascular system. Insufficient Magnesium levels can trigger Vasoconstriction and exacerbate Endothelial Damage in blood vessels, hence promoting the progression and deterioration of Atherosclerosis. The study aims to examine the Serum Magnesium levels in the participants, assess the short-term improvement and outcome upon discharge amoung Acute Ischemic Stroke patients, and establish the association between Serum Magnesium levels and Short-Term Outcome in Acute Ischemic Stroke patients. Materials and Methods: 50 patients diagnosed with acute ischemic stroke using MRI brain were included. The NIHSS Score was utilized to evaluate the severity of an Ischemic Stroke. Serum Magnesium levels were assessed via blood tests and then compared to the Short Term Outcome of the study participants. Results were tabulated and analyzed. Result: Mean (SD) age of the patients was 64.56 (6.25) years. 11 (22%) were females and 39 (78%) males. 46 (92%) patients had NIHSS score less than 10 and 4 (8%) patients had NIHSS score more than 10. Mean (SD) Serum Magnesium concentration was significantly higher in patients with NIHSS less than 10 (p<0.0001). NIHSS score was inversely related to magnesium concentration (r=-0.3; p=0.02). Conclusion: Individuals with acute ischemic stroke who had a higher concentration of magnesium in their blood had a decreased likelihood of having a National Institutes of Health Stroke Scale (NIHSS) score of 10 or higher.

# **INTRODUCTION**

Stroke ranks as the third leading cause of mortality and chronic impairment on a global scale. It is probable that the occurrence of Stroke will rise in the upcoming two decades.<sup>[1]</sup> Acute Ischemic Stroke comprises 60% of all strokes and is associated with a greater death and disability rate. Therefore, the longterm outlook of Acute Ischemic Stroke is a significant concern.<sup>[2]</sup> The possible neuroprotective impact of Magnesium was examined, and a previous case-control study indicated that maintaining an adequate amount of dietary Magnesium could be advantageous in averting Ischemic Stroke.<sup>[3]</sup> In addition, a meta-analysis of 7 prospective studies revealed a small yet statistically significant inverse correlation between Magnesium consumption and the likelihood of experiencing Acute Ischemic Stroke.<sup>[4]</sup>

A recent study discovered that there is a negative correlation between Serum Magnesium

concentration and the occurrence of Ischemic Stroke. Magnesium (Mg) exerts significant effects on the vascular system. Research has demonstrated that a lack of Magnesium can initiate vasoconstriction and intensify damage to the blood vessels' inner lining, hence facilitating the advancement and worsening of atherosclerosis.<sup>[5]</sup> Nevertheless, there is still limited comprehension regarding the potential role of low Serum Magnesium in promoting the onset of stroke. The objective of the study is to assess the Serum Magnesium levels in the participants, evaluate the short-term improvement and outcome upon discharge, and determine the correlation between Serum Magnesium levels and short-term outcome in the participants.

### **MATERIALS AND METHODS**

**Study design and participants:** This study was conducted at the General Medicine department of an academic tertiary care institution, using a hospital-

based cross-sectional analytical design. The study included individuals diagnosed with Acute Ischemic Stroke. The study excluded patients diagnosed with Addison's disease, Dehydration, Renal failure, and patients undergoing Lithium therapy. The study received approval from the institutional ethical committee. The patients provided signed consent after being fully informed.

**Outcomes and measures:** A total of 50 patients were enrolled in this trial. A comprehensive medical history was obtained and a thorough clinical examination was conducted. The patient was diagnosed with Acute Ischemic Stroke using MRI of the Brain. The NIHSS (National Institute of Health Stroke Scale) Score is utilized to evaluate the severity of an Ischemic Stroke. Serum Magnesium levels were assessed via blood tests and then compared to the Short Term Outcome of the study participants.

**Statistical analysis:** The data acquired were inputted into Microsoft Excel sheets 2010 and analyzed using Epi Info v3.0 statistical software. The descriptive statistics were evaluated to determine measures of central tendency and dispersion. The results were then displayed using tables, bar diagrams, graphs, and other visual representations. Logistic Regression was employed to analyze the inferential statistics. A p-value less than 0.05 was deemed to be statistically significant.

#### RESULTS

**Demographic data:** Mean (SD) age of the patients was 64.56 (6.25) years. 11 (22%) were females and 39 (78%) males. 46 (92%) patients had NIHSS score less than 10 and 4 (8%) patients had NIHSS score more than 10. Table I displays the demographic and clinical features of patients upon admission, categorized based on their NIHSS score being either greater than 10 or less than 10. We included a total of 50 cases of Acute Ischemic Stroke in our investigation. Patients with a National Institutes of Health Stroke Scale (NIHSS) score of less than 10 had a greater likelihood of having elevated levels of Magnesium in their blood serum. There were no notable disparities in age, gender, Serum Calcium levels, serum Potassium levels, admission SBP, DBP,

Total Cholesterol (TC), Triglycerides (TG), Low-Density Lipoprotein cholesterol (LDL-C), High-Density Lipoprotein cholesterol (HDL-C), history of Hypertension, and history of Diabetes.

Serum Magnesium concentration: Mean (SD) Serum Magnesium concentration was 0.89 (0.05) mmol/l. Mean (SD) Serum Magnesium among patients with NIHSS Score less than 10 was 0.89 (0.05) and in NIHSS Score more than 10 was 0.84 (0.01). It was significantly higher in patients with NIHSS Score less than 10 (p<0.0001).

**Serum Magnesium concentration and NIHSS score:** Mean (SD) NIHSS Score among those with NIHSS Score less than 10 was 6.24 (1.77) and mean (SD) NIHSS Score among those with NIHSS Score more than 10 was 16.25 (2.99). NIHSS Score was inversely related to Serum Magnesium concentration. When Serum Magnesium concentration was high, NIHSS Score was low (r=-0.3; p=0.02).

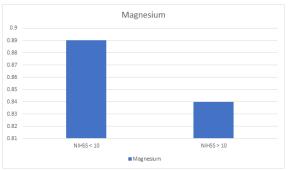
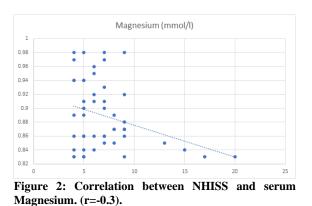


Figure 1. Serum Magnesium level and NHISS



Characteristic	NIHSS<10		NIHSS>10		р
	Mean	SD	Mean	SD	
n	46		4		
Age	64.43	6.37	66.00	5.23	0.6044
M:F	39:9	39:9		2:2	
NIHSS score	6.24	1.77	16.25	2.99	0.0059
Magnesium (mmol/l)	0.89	0.05	0.84	0.01	< 0.0001
Calcium (mmol/l)	2.33	0.06	2.29	0.05	0.1996
Potassium (mmol/l)	4.08	0.22	4.18	0.26	0.5300
SBP	143.78	14.95	156.50	12.48	0.1309
DBP	88.87	7.54	79.50	5.74	0.0388
Hypertension	67%	67%		75%	
DM	24%	24%		25%	
Total Cholesterol (mmol/l)	1.37	0.26	1.47	0.31	0.5537
TG (mmol/l)	4.91	0.36	4.74	0.38	0.4335
LDL (mmol/l)	2.99	0.35	2.76	0.22	0.1246

HDL (mmol/l)	1.26	0.13	1.30	0.09	0.4618
FBS (mmol/l)	5.94	0.56	5.71	0.73	0.5748
Days hospitalized	16.11	3.14	18.25	3.20	0.2768

# DISCUSSION

The results of our investigation revealed a strong and statistically significant relationship between the concentration of Serum Magnesium in the blood serum and the short-term outcome. A cross-sectional investigation indicated a potential association between low Serum Magnesium concentrations and Cardiovascular Disease.6 Amighi et al.'s cohort study discovered a correlation between low levels of Serum Magnesium in the blood and the occurrence of neurological events, particularly ischemic stroke, among individuals with advanced atherosclerosis.7 A further study demonstrated that having a low level of Serum Magnesium in the blood was linked to a higher chance of experiencing an Ischemic Stroke. However, this correlation lost its significance after taking into account the presence of Hypertension and Diabetes.8 A male participants prospective analysis revealed that there was no correlation between dietary Magnesium intake and Cardiovascular mortality.9 However, it is important to note that the study did not consider Hypertension and other related factors. A prospective study indicated that individuals with low levels of Serum Magnesium in their blood had a higher risk of death from any cause and from Cardiovascular-related causes.10 The relationship remained statistically significant even after accounting for other cardiovascular risk factors, including high Blood Pressure and medications used to treat it.[11]

The majority of Magnesium in the body of an adult is located in connective tissue, bones, and organs, whereas only 1% is found in the bloodstream. While serum Magnesium only represents a small portion of the overall Magnesium in the body of an individual, it is frequently utilized as a biomarker in clinical settings to evaluate the state of Magnesium metabolism.<sup>[12]</sup> A direct relationship exists between the concentration of Magnesium in the blood and the amount of Magnesium consumed through diet. Metaanalytic epidemiological studies have demonstrated a correlation between dietary Magnesium intake with a decrease in the likelihood of Stroke, Cardiovascular mortality, and enhanced Neurological functioning in Stroke patients after discharge.<sup>[13]</sup>

The precise pathophysiological mechanism underlying the relationship between low Serum Magnesium levels and poststroke impairment is still not fully understood. Nevertheless, the complete demonstration of Magnesium's potential as a neuroprotective drug in cases of Acute Ischemic Stroke was established. Researchers put out multiple hypotheses.<sup>[14]</sup> Initially, Serum Magnesium can function as a Biomarker for certain pre-Stroke pathological conditions that significantly impact the prognosis, such as Hypertension, Hyperglycemia, and severe Renal insufficiency. These are recognized risk factors that influence the prognosis and mortality of Stroke.<sup>[15]</sup>

Additionally, a lack of Magnesium can cause the inflammatory system to become active, potentially by activating NF-kB. This activation can lead to the creation of pro-inflammatory phenotypes, resulting in damage and dysfunction of the vascular endothelium. This, in turn, leads to the formation and progression of atherosclerotic lesions, which then triggers vascular calcification alongside encourages the buildup of lipids in vascular plaques.<sup>[16]</sup> Furthermore, there is a direct correlation between Magnesium deficiency and the occurrence of Thrombosis, as platelet activation serves as the underlying cause of Thrombosis. Serum Magnesium can stimulate the elimination of platelet inhibitor pgi230 while enhancing the breakdown of Hypervascular Hemophilia factors (prethrombotic glycoprotein), thus preventing platelet adhesion as well as aggregation.<sup>[17]</sup>

Prior research has demonstrated that decreased levels of Magnesium have a notable impact on plateletdependent Thrombosis in individuals diagnosed with stable Coronary heart disease. Additionally, a deficiency in Magnesium can heighten oxidative stress as well as chronic inflammation, both of which are significant factors in the aging of the brain and the decrease of cognitive function. This can ultimately result in compromised survival and hindered functional recovery.<sup>[18]</sup>

This study had multiple limitations. It is possible that there are residual confounders present in this present observational study. Thus, we are unable to establish a definitive cause-and-effect connection between Magnesium with outcomes. Furthermore, we only possess a solitary Serum Magnesium measurement taken at the beginning of the study, with no subsequent measurements taken to track changes over time. Consequently, we are unable to assess the impact of fluctuating levels of Serum Magnesium on negative outcomes of stroke. This information could offer useful insights into the underlying mechanisms of these correlations. Diuretic therapy for Hypertension can lead to a decrease in the concentration of Serum Magnesium.19 Furthermore, the absence of information regarding nutrients or dietarv components associated with Serum Magnesium concentration is likely to result in an underestimated correlation.

# **CONCLUSION**

To summarize, the current investigation indicated that a higher level of Serum Magnesium was linked to a reduced likelihood of having a National Institutes of Health Stroke Scale (NIHSS) score more than 10 in individuals with Acute Ischemic Stroke.

#### REFERENCES

- Mukherjee D, Patil CG. Epidemiology and the global burden of stroke. World neurosurgery. 2011 Dec 1;76(6):S85-90.
   Saini V, Guada L, Yavagal DR. Global epidemiology of stroke
- Saini V, Guada L, Yavagal DR. Global epidemiology of stroke and access to acute ischemic stroke interventions. Neurology. 2021 Nov 16;97(20\_Supplement\_2):S6-16.
- Yang L, Chen X, Cheng H, Zhang L. Dietary copper intake and risk of stroke in adults: a case-control study based on national health and nutrition examination survey 2013–2018. Nutrients. 2022 Jan 18;14(3):409.
- Del Gobbo LC, Imamura F, Wu JH, de Oliveira Otto MC, Chiuve SE, Mozaffarian D. Circulating and dietary magnesium and risk of cardiovascular disease: a systematic review and meta-analysis of prospective studies. The American journal of clinical nutrition. 2013 Jul 1;98(1):160-73.
- Feng P, Niu X, Hu J, Zhou M, Liang H, Zhang Y, Tong W, Xu T. Relationship of serum magnesium concentration to risk of short-term outcome of acute ischemic stroke. Blood Pressure. 2013 Oct 1;22(5):297-301.
- Cojocaru IM, Cojocaru M, Burcin C, Atanasiu NA. Serum magnesium in patients with acute ischemic stroke. Romanian journal of internal medicine= Revue roumaine de medecine interne. 2007 Jan 1;45(3):269-73.
- Amighi J, Sabeti S, Schlager O, Mlekusch W, Exner M, Lalouschek W, Ahmadi R, Minar E, Schillinger M. Low serum magnesium predicts neurological events in patients with advanced atherosclerosis. Stroke. 2004 Jan 1;35(1):22-7.
- Larsson SC, Traylor M, Burgess S, Boncoraglio GB, Jern C, Michaëlsson K, Markus HS, MEGASTROKE project of the International Stroke Genetics Consortium, MEGASTROKE project of the International Stroke Genetics Consortium. Serum magnesium and calcium levels in relation to ischemic stroke: Mendelian randomization study. Neurology. 2019 Feb 26;92(9):e944-50.
- Xu Q, Hu L, Chen L, Li H, Tian X, Zuo Y, Zhang Y, Zhang X, Sun P, Wang Y, Meng X. Low serum magnesium is associated with poor functional outcome in acute ischemic stroke or transient ischemic attack patients. CNS Neuroscience & Therapeutics. 2023 Mar;29(3):842-54.
- Reffelmann T, Ittermann T, Dörr M, Völzke H, Reinthaler M, Petersmann A, Felix SB. Low serum magnesium concentrations predict cardiovascular and all-cause mortality. Atherosclerosis. 2011 Nov 1;219(1):280-4.

- Ohira T, Peacock JM, Iso H, Chambless LE, Rosamond WD, Folsom AR. Serum and dietary magnesium and risk of ischemic stroke: the Atherosclerosis Risk in Communities Study. American journal of epidemiology. 2009 Jun 15;169(12):1437-44.
- Long S, Romani AM. Role of cellular magnesium in human diseases. Austin journal of nutrition and food sciences. 2014 Nov 18;2(10).
- 13. Pan WH, Lai YH, Yeh WT, Chen JR, Jeng JS, Bai CH, Lin RT, Lee TH, Chang KC, Lin HJ, Hsiao CF. Intake of potassium-and magnesium-enriched salt improves functional outcome after stroke: a randomized, multicenter, double-blind controlled trial. The American journal of clinical nutrition. 2017 Nov 1;106(5):1267-73.
- 14. Shah N, Sethi R, Shah S, Jafri K, Duran J, Chang Y, Soni C, Wollocko H. The roles of platelet-activating factor and magnesium in pathophysiology of hypertension, atherogenesis, cardiovascular disease, stroke and aging. Cardiogenetics. 2022 Feb 2;12(1):49-62.
- Turek-Jakubowska A, Dębski J, Jakubowski M, Szahidewicz-Krupska E, Gawryś J, Gawryś K, Janus A, Trocha M, Doroszko A. New Candidates for Biomarkers and Drug Targets of Ischemic Stroke—A First Dynamic LC-MS Human Serum Proteomic Study. Journal of Clinical Medicine. 2022 Jan 11;11(2):339.
- 16. Ashique S, Kumar S, Hussain A, Mishra N, Garg A, Gowda BJ, Farid A, Gupta G, Dua K, Taghizadeh-Hesary F. A narrative review on the role of magnesium in immune regulation, inflammation, infectious diseases, and cancer. Journal of Health, Population and Nutrition. 2023 Jul 27;42(1):74.
- Mazur A, Maier JA, Rock E, Gueux E, Nowacki W, Rayssiguier Y. Magnesium and the inflammatory response: potential physiopathological implications. Archives of biochemistry and biophysics. 2007 Feb 1;458(1):48-56.
- Shechter M, Sharir M, Labrador MJ, Forrester J, Silver B, Bairey Merz CN. Oral magnesium therapy improves endothelial function in patients with coronary artery disease. Circulation. 2000 Nov 7;102(19):2353-8.
- Guerrero-Romero F, Rodríguez-Morán M. The effect of lowering blood pressure by magnesium supplementation in diabetic hypertensive adults with low serum magnesium levels: a randomized, double-blind, placebo-controlled clinical trial. Journal of human hypertension. 2009 Apr;23(4):245-51.